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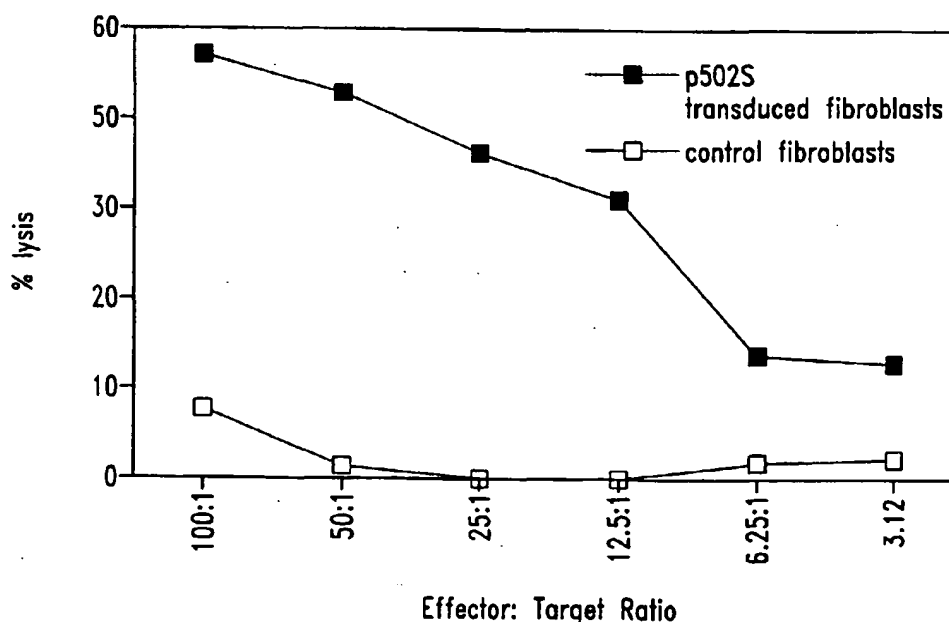
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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.

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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of
5 cancer, such as prostate cancer. The invention is more specifically related to
polypeptides, comprising at least a portion of a prostate-specific protein, and to
polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides
are useful in pharmaceutical compositions, *e.g.*, vaccines, and other compositions for
the diagnosis and treatment of prostate cancer.

10 BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although
Cancer is a significant health problem throughout the world. Although advances have
been made in detection and therapy of cancer, no vaccine or other universally successful
method for prevention or treatment is currently available. Current therapies, which are
15 generally based on a combination of chemotherapy or surgery and radiation, continue to
prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with
an estimated incidence of 30% in men over the age of 50. Overwhelming clinical
evidence shows that human prostate cancer has the propensity to metastasize to bone,
20 and the disease appears to progress inevitably from androgen dependent to androgen
refractory status, leading to increased patient mortality. This prevalent disease is
currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate
cancer remains difficult to treat. Commonly, treatment is based on surgery and/or
25 radiation therapy, but these methods are ineffective in a significant percentage of cases.
Two previously identified prostate specific proteins - prostate specific antigen (PSA)
and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic
potential. For example, PSA levels do not always correlate well with the presence of

prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other
5 cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide
10 compositions comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and
15 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-
20 931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;
25

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-

606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of prostate tissue samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for other normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855,

858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858 or 860-862, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant, together with a physiologically acceptable carrier.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

5 Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10 Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

 The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides
15 encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating and/or enhancing the expression,
20 purification and/or immunogenicity of the polypeptide(s).

 Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with prostate cancer, in which case the methods provide
25 treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition as recited above. The patient may be afflicted

with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological
5 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the polypeptide from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological
10 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen presenting cell that
15 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a
20 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a
25 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for
30 determining the presence or absence of a cancer, preferably a prostate cancer, in a

patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide of the present invention, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to an inventive polynucleotide, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample

obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

5 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

10 Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

15 Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25 Figure 11 shows the results of an ELISA assay to determine the specificity of rabbit polyclonal antisera raised against P501S.

Figures 12A(1), 12A(2), 12A(3), and B are the full-length cDNA (SEQ ID NO:777) and predicted amino acid (SEQ ID NO:778) sequences, respectively, for the clone P788P.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

30 SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
5 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
10 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
15 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
20 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
25 SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
30 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21

SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
5 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861
SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864
SEQ ID NO: 41 is the determined cDNA sequence for P5
10 SEQ ID NO: 42 is the determined cDNA sequence for P8
SEQ ID NO: 43 is the determined cDNA sequence for P9
SEQ ID NO: 44 is the determined cDNA sequence for P18
SEQ ID NO: 45 is the determined cDNA sequence for P20
SEQ ID NO: 46 is the determined cDNA sequence for P29
15 SEQ ID NO: 47 is the determined cDNA sequence for P30
SEQ ID NO: 48 is the determined cDNA sequence for P34
SEQ ID NO: 49 is the determined cDNA sequence for P36
SEQ ID NO: 50 is the determined cDNA sequence for P38
SEQ ID NO: 51 is the determined cDNA sequence for P39
20 SEQ ID NO: 52 is the determined cDNA sequence for P42
SEQ ID NO: 53 is the determined cDNA sequence for P47
SEQ ID NO: 54 is the determined cDNA sequence for P49
SEQ ID NO: 55 is the determined cDNA sequence for P50
SEQ ID NO: 56 is the determined cDNA sequence for P53
25 SEQ ID NO: 57 is the determined cDNA sequence for P55
SEQ ID NO: 58 is the determined cDNA sequence for P60
SEQ ID NO: 59 is the determined cDNA sequence for P64
SEQ ID NO: 60 is the determined cDNA sequence for P65
SEQ ID NO: 61 is the determined cDNA sequence for P73
30 SEQ ID NO: 62 is the determined cDNA sequence for P75

SEQ ID NO: 63 is the determined cDNA sequence for P76

SEQ ID NO: 64 is the determined cDNA sequence for P79

SEQ ID NO: 65 is the determined cDNA sequence for P84

SEQ ID NO: 66 is the determined cDNA sequence for P68

5 SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred
to as P704P)

SEQ ID NO: 68 is the determined cDNA sequence for P82

SEQ ID NO: 69 is the determined cDNA sequence for U1-3064

SEQ ID NO: 70 is the determined cDNA sequence for U1-3065

10 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692

SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905

SEQ ID NO: 73 is the determined cDNA sequence for V1-3686

SEQ ID NO: 74 is the determined cDNA sequence for R1-2330

SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976

15 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736

SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738

SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741

SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744

20 SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734

SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774

SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781

SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785

SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787

25 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796

SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807

SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810

SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811

SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876

30 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

- SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896
- SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761
- SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762
- SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766
- 5 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770
- SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771
- SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772
- SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297
- SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309
- 10 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278
- SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288
- SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283
- SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
- SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
- 15 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
- SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12
(also referred to as P504S)
- SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
- SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
- 20 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12
(also referred to as P501S)
- SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as P503S)
- SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
- 25 SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)
- SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)
- SEQ ID NO: 115 is the determined cDNA sequence for P89
- 30 SEQ ID NO: 116 is the determined cDNA sequence for P90

SEQ ID NO: 117 is the determined cDNA sequence for P92
SEQ ID NO: 118 is the determined cDNA sequence for P95
SEQ ID NO: 119 is the determined cDNA sequence for P98
SEQ ID NO: 120 is the determined cDNA sequence for P102
5 SEQ ID NO: 121 is the determined cDNA sequence for P110
SEQ ID NO: 122 is the determined cDNA sequence for P111
SEQ ID NO: 123 is the determined cDNA sequence for P114
SEQ ID NO: 124 is the determined cDNA sequence for P115
SEQ ID NO: 125 is the determined cDNA sequence for P116
10 SEQ ID NO: 126 is the determined cDNA sequence for P124
SEQ ID NO: 127 is the determined cDNA sequence for P126
SEQ ID NO: 128 is the determined cDNA sequence for P130
SEQ ID NO: 129 is the determined cDNA sequence for P133
SEQ ID NO: 130 is the determined cDNA sequence for P138
15 SEQ ID NO: 131 is the determined cDNA sequence for P143
SEQ ID NO: 132 is the determined cDNA sequence for P151
SEQ ID NO: 133 is the determined cDNA sequence for P156
SEQ ID NO: 134 is the determined cDNA sequence for P157
SEQ ID NO: 135 is the determined cDNA sequence for P166
20 SEQ ID NO: 136 is the determined cDNA sequence for P176
SEQ ID NO: 137 is the determined cDNA sequence for P178
SEQ ID NO: 138 is the determined cDNA sequence for P179
SEQ ID NO: 139 is the determined cDNA sequence for P185
SEQ ID NO: 140 is the determined cDNA sequence for P192
25 SEQ ID NO: 141 is the determined cDNA sequence for P201
SEQ ID NO: 142 is the determined cDNA sequence for P204
SEQ ID NO: 143 is the determined cDNA sequence for P208
SEQ ID NO: 144 is the determined cDNA sequence for P211
SEQ ID NO: 145 is the determined cDNA sequence for P213
30 SEQ ID NO: 146 is the determined cDNA sequence for P219

SEQ ID NO: 147 is the determined cDNA sequence for P237
SEQ ID NO: 148 is the determined cDNA sequence for P239
SEQ ID NO: 149 is the determined cDNA sequence for P248
SEQ ID NO: 150 is the determined cDNA sequence for P251
5 SEQ ID NO: 151 is the determined cDNA sequence for P255
SEQ ID NO: 152 is the determined cDNA sequence for P256
SEQ ID NO: 153 is the determined cDNA sequence for P259
SEQ ID NO: 154 is the determined cDNA sequence for P260
SEQ ID NO: 155 is the determined cDNA sequence for P263
10 SEQ ID NO: 156 is the determined cDNA sequence for P264
SEQ ID NO: 157 is the determined cDNA sequence for P266
SEQ ID NO: 158 is the determined cDNA sequence for P270
SEQ ID NO: 159 is the determined cDNA sequence for P272
SEQ ID NO: 160 is the determined cDNA sequence for P278
15 SEQ ID NO: 161 is the determined cDNA sequence for P105
SEQ ID NO: 162 is the determined cDNA sequence for P107
SEQ ID NO: 163 is the determined cDNA sequence for P137
SEQ ID NO: 164 is the determined cDNA sequence for P194
SEQ ID NO: 165 is the determined cDNA sequence for P195
20 SEQ ID NO: 166 is the determined cDNA sequence for P196
SEQ ID NO: 167 is the determined cDNA sequence for P220
SEQ ID NO: 168 is the determined cDNA sequence for P234
SEQ ID NO: 169 is the determined cDNA sequence for P235
SEQ ID NO: 170 is the determined cDNA sequence for P243
25 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13
30 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13

SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14

SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-

4736

5 SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-

4738

SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-

4741

SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-

10 4744

SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-

4774

SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-

4781

15 SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-

4785

SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-

4787

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-

20 4796

SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-

4807

SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810

SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811

25 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-

4876

SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-

4884

SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-

30 4896

SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-
4761

SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-
4762

5 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-
4766

SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770
SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-
10 4772

SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-
4309

SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-
4278

15 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-
4288

SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-
4283

SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-
20 4304

SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-
4296

SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-
4280

25 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
30 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
5 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
10 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
SEQ ID NO: 223 is the determined cDNA sequence for P509S
SEQ ID NO: 224 is the determined cDNA sequence for P510S
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
15 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23
20 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
25 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
30 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42

SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
5 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
10 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
15 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3
20 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
25 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
30 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
5 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
10 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
15 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
20 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
25 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
30 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

- SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
5 SEQ ID NO: 307 is the determined cDNA sequence for P711P
SEQ ID NO: 308 is the determined cDNA sequence for P712P
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
SEQ ID NO: 310 is the determined cDNA sequence for P774P
SEQ ID NO: 311 is the determined cDNA sequence for P775P
10 SEQ ID NO: 312 is the determined cDNA sequence for P715P
SEQ ID NO: 313 is the determined cDNA sequence for P710P
SEQ ID NO: 314 is the determined cDNA sequence for P767P
SEQ ID NO: 315 is the determined cDNA sequence for P768P
SEQ ID NO: 316-325 are the determined cDNA sequences of previously
15 isolated genes
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
20 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
SEQ ID NO: 332 is the determined full length cDNA sequence for
P509S
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P
25 (also referred to as 11-C9)
SEQ ID NO: 334 is the determined cDNA sequence for P714P
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also
referred to as 9-F3)
SEQ ID NO: 336 is the predicted amino acid sequence for P705P
30 SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- 5 SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing
homology to Homo sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing
homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- 10 SEQ ID NO: 345 is the determined cDNA sequence for a clone showing
homology to Homo sapiens mRNA for E-cadherin
- SEQ ID NO: 346 is the determined cDNA sequence for a clone showing
homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase
(SHMT)
- 15 SEQ ID NO: 347 is the determined cDNA sequence for a clone showing
homology to Homo sapiens natural resistance-associated macrophage protein2
(NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing
homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)
- 20 SEQ ID NO: 349 is the determined cDNA sequence for a clone showing
homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- SEQ ID NO: 352 is the determined cDNA sequence for P790P
- 25 SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- SEQ ID NO: 357 is the determined cDNA sequence for P745S
- 30 SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

5 SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

10 SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

15 SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

20 SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

25 SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO: 386 is the cDNA sequence for 23320.

SEQ ID NO: 387 is the cDNA sequence for CGI-69.

SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO: 389 is the cDNA sequence for 23379.

30 SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

5 SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor
PDEF.

10 SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

15 SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553 (also known as
P1020C).

20 SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

25 SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

30 SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.
SEQ ID NO:420 is the cDNA sequence for 22581.
SEQ ID NO:421 is the cDNA sequence for 22582.
SEQ ID NO:422 is the cDNA sequence for 22583.
5 SEQ ID NO:423 is the cDNA sequence for 22584.
SEQ ID NO:424 is the cDNA sequence for 22585.
SEQ ID NO:425 is the cDNA sequence for 22586.
SEQ ID NO:426 is the cDNA sequence for 22587.
SEQ ID NO:427 is the cDNA sequence for 22588.
10 SEQ ID NO:428 is the cDNA sequence for 22589.
SEQ ID NO:429 is the cDNA sequence for 22590.
SEQ ID NO:430 is the cDNA sequence for 22591.
SEQ ID NO:431 is the cDNA sequence for 22592.
SEQ ID NO:432 is the cDNA sequence for 22593.
15 SEQ ID NO:433 is the cDNA sequence for 22594.
SEQ ID NO:434 is the cDNA sequence for 22595.
SEQ ID NO:435 is the cDNA sequence for 22596.
SEQ ID NO:436 is the cDNA sequence for 22847.
SEQ ID NO:437 is the cDNA sequence for 22848.
20 SEQ ID NO:438 is the cDNA sequence for 22849.
SEQ ID NO:439 is the cDNA sequence for 22851.
SEQ ID NO:440 is the cDNA sequence for 22852.
SEQ ID NO:441 is the cDNA sequence for 22853.
SEQ ID NO:442 is the cDNA sequence for 22854.
25 SEQ ID NO:443 is the cDNA sequence for 22855.
SEQ ID NO:444 is the cDNA sequence for 22856.
SEQ ID NO:445 is the cDNA sequence for 22857.
SEQ ID NO:446 is the cDNA sequence for 23601.
SEQ ID NO:447 is the cDNA sequence for 23602.
30 SEQ ID NO:448 is the cDNA sequence for 23605.

- SEQ ID NO:449 is the cDNA sequence for 23606.
- SEQ ID NO:450 is the cDNA sequence for 23612.
- SEQ ID NO:451 is the cDNA sequence for 23614.
- SEQ ID NO:452 is the cDNA sequence for 23618.
- 5 SEQ ID NO:453 is the cDNA sequence for 23622.
- SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
- SEQ ID NO:455 is the cDNA sequence for LIM protein.
- SEQ ID NO:456 is the cDNA sequence for a known gene.
- SEQ ID NO:457 is the cDNA sequence for a known gene.
- 10 SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:459 is the cDNA sequence for 23045.
- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for clone 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- 15 SEQ ID NO:468-471 are cDNA sequences for P710P.
- SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 20 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- 25 SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 30

SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

5 SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

10 SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

15 SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

20 SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

25 SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

30 SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.

SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

5 SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

10 SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

15 SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

20 SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

25 SEQ ID NO: 552 is an extended cDNA sequence for P712P.

SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.

SEQ ID NO: 569 is an extended cDNA sequence for P776P.

30 SEQ ID NO: 570 is the determined cDNA sequence for a splice variant of P776P referred to as contig 6.

SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

5 SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

10 SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

15 SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

20 SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

SEQ ID NO: 594 is a splice variant of P775P referred to as 50717. SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

25 SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

30 SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

5 SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P
and PSA.

SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and
PSA.

10 SEQ ID NO: 618-689 are determined cDNA sequences of prostate-
specific clones.

SEQ ID NO: 690 is the cDNA sequence of the gene DD3.

SEQ ID NO: 691-697 are determined cDNA sequences of prostate-
specific clones.

SEQ ID NO: 698 is an extended cDNA sequence for P714P.

15 SEQ ID NO: 699-701 are the cDNA sequences for splice variants of
P704P.

SEQ ID NO: 702 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-14.

20 SEQ ID NO: 703 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-12.

SEQ ID NO: 704 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-10.

SEQ ID NO: 705 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-6.

25 SEQ ID NO: 706 is the amino acid sequence encoded by SEQ ID NO:
705.

SEQ ID NO: 707 is the amino acid sequence encoded by SEQ ID NO:
702 SEQ ID NO: 708 is a second amino acid sequence encoded by SEQ ID NO: 702.

30 SEQ ID NO: 709-772 are determined cDNA sequences of prostate-
specific clones.

SEQ ID NO: 773 is a first full-length cDNA sequence for prostate-specific transglutaminase gene (also referred to herein as P558S).

SEQ ID NO: 774 is a second full-length cDNA sequence for prostate-specific transglutaminase gene.

5 SEQ ID NO: 775 is the amino acid sequence encoded by the sequence of
SEQ ID NO: 773.

SEQ ID NO: 776 is the amino acid sequence encoded by the sequence of SEQ ID NO: 774.

SEQ ID NO: 777 is the full-length cDNA sequence for P788P.

10 SEQ ID NO: 778 is the amino acid sequence encoded by SEQ ID NO:
777.

SEQ ID NO: 779 is the determined cDNA sequence for a polymorphic variant of P788P.

SEQ ID NO: 780 is the amino acid sequence encoded by SEQ ID NO: 15 779.

SEQ ID NO: 781 is the amino acid sequence of peptide 4 from P703P.

SEQ ID NO: 782 is the cDNA sequence that encodes peptide 4 from P703P.

SEQ ID NO: 783-798 are the cDNA sequence encoding epitopes of
20 P703P.

SEQ ID NO: 799-814 are the amino acid sequences of epitopes of P703P.

SEQ ID NO: 815 and 816 are PCR primers.

SEQ ID NO: 817 is the cDNA sequence encoding an N-terminal portion
25 of P788P expressed in *E. coli*.

SEQ ID NO: 818 is the amino acid sequence of the N-terminal portion of P788P expressed in *E. coli*.

SEQ ID NO: 819 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

30 SEQ ID NO: 820 and 821 are PCR primers.

SEQ ID NO: 822 is the cDNA sequence for the Ra12-P510S-C construct.

SEQ ID NO: 823 is the cDNA sequence for the P510S-C construct.

SEQ ID NO: 824 is the cDNA sequence for the P510S-E3 construct.

5 SEQ ID NO: 825 is the amino acid sequence for the Ra12-P510S-C construct.

SEQ ID NO: 826 is the amino acid sequence for the P510S-C construct.

SEQ ID NO: 827 is the amino acid sequence for the P510S-E3 construct.

SEQ ID NO: 828-833 are PCR primers.

10 SEQ ID NO: 834 is the cDNA sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 835 is the amino acid sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 836 and 837 are PCR primers.

15 SEQ ID NO: 838 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 839 is the determined cDNA sequence for a P703P His tag fusion protein.

SEQ ID NO: 840 and 841 are PCR primers.

20 SEQ ID NO: 842 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 843 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 844 and 845 are PCR primers.

25 SEQ ID NO: 846 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 847 is the determined cDNA sequence for a P711P His tag fusion protein.

30 SEQ ID NO: 848 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 849 and 850 are PCR primers.

SEQ ID NO: 851 is the determined cDNA sequence for the construct Ra12-P501S-E2.

5 SEQ ID NO: 852 is the determined amino acid sequence for the construct Ra12-P501S-E2.

SEQ ID NO: 853 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 854 is the DNA sequence encoding SEQ ID NO: 853.

SEQ ID NO: 855 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 856 is the DNA sequence encoding SEQ ID NO: 855.

10 SEQ ID NO: 857 is a peptide employed in epitope mapping studies.

SEQ ID NO: 858 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 859 is the DNA sequence encoding SEQ ID NO: 858.

SEQ ID NO: 860-862 are the amino acid sequences for CD4 epitopes of P501S.

15 SEQ ID NO: 863-865 are the DNA sequences encoding the sequences of SEQ ID NO: 860-862.

SEQ ID NO: 866-877 are the amino acid sequences for putative CTL epitopes of P703P.

SEQ ID NO: 878 is the full-length cDNA sequence for P789P.

20 SEQ ID NO: 879 is the amino acid sequence encoded by SEQ ID NO: 878.

SEQ ID NO: 880 is the determined full-length cDNA sequence for the splice variant of P776P referred to as contig 6.

25 SEQ ID NO: 881-882 are determined full-length cDNA sequences for the splice variant of P776P referred to as contig 7.

SEQ ID NO: 883-887 are amino acid sequences encoded by SEQ ID NO: 880.

SEQ ID NO: 888-893 are amino acid sequences encoded by the splice variant of P776P referred to as contig 7.

SEQ ID NO: 894 is the full-length cDNA sequence for human transmembrane protease serine 2.

SEQ ID NO: 895 is the amino acid sequence encoded by SEQ ID NO: 894.

5 SEQ ID NO: 896 is the cDNA sequence encoding the first 209 amino acids of human transmembrane protease serine 2.

SEQ ID NO: 897 is the first 209 amino acids of human transmembrane protease serine 2.

10 SEQ ID NO: 898 is the amino acid sequence of peptide 296-322 of P501S.

SEQ ID NO: 899-902 are PCR primers.

SEQ ID NO: 903 is the determined cDNA sequence of the Vb chain of a T cell receptor for the P501S-specific T cell clone 4E5.

15 SEQ ID NO: 904 is the determined cDNA sequence of the Va chain of a T cell receptor for the P501S-specific T cell clone 4E5.

SEQ ID NO: 905 is the amino acid sequence encoded by SEQ ID NO 903.

SEQ ID NO: 906 is the amino acid sequence encoded by SEQ ID NO 904.

20 SEQ ID NO: 907 is the full-length open reading frame for P768P including stop codon.

SEQ ID NO: 908 is the full-length open reading frame for P768P without stop codon.

25 SEQ ID NO: 909 is the amino acid sequence encoded by SEQ ID NO: 908.

SEQ ID NO: 910-915 are the amino acid sequences for predicted domains of P768P.

SEQ ID NO: 916 is the full-length cDNA sequence of P835P.

30 SEQ ID NO: 917 is the cDNA sequence of the previously identified clone FLJ13581.

SEQ ID NO: 918 is the cDNA sequence of the open reading frame for P835P with stop codon.

SEQ ID NO: 919 is the cDNA sequence of the open reading frame for P835P without stop codon.

5 SEQ ID NO: 920 is the full-length amino acid sequence for P835P.

SEQ ID NO: 921-928 are the amino acid sequences of extracellular and intracellular domains of P835P.

SEQ ID NO: 929 is the full-length cDNA sequence for P1000C.

10 SEQ ID NO: 930 is the cDNA sequence of the open reading frame for P1000C, including stop codon.

SEQ ID NO: 931 is the cDNA sequence of the open reading frame for P1000C, without stop codon.

SEQ ID NO: 932 is the full-length amino acid sequence for P1000C.

SEQ ID NO: 933 is amino acids 1-100 of SEQ ID NO: 932.

15 SEQ ID NO: 934 is amino acids 100-492 of SEQ ID NO: 932.

SEQ ID NO: 935-937 are PCR primers.

SEQ ID NO: 938 is the cDNA sequence of the expressed full-length P767P coding region.

20 SEQ ID NO: 939 is the cDNA sequence of an expressed truncated P767P coding region.

SEQ ID NO: 940 is the amino acid sequence encoded by SEQ ID NO: 939.

SEQ ID NO: 941 is the amino acid sequence encoded by SEQ ID NO: 938.

25 SEQ ID NO: 942 is the DNA sequence of a CD4 epitope of P703P.

SEQ ID NO: 943 is the amino acid sequence of a CD4 epitope of P703P.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly prostate cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); Maniatis et al. *Molecular Cloning: A Laboratory Manual* (1982); *DNA Cloning: A Practical Approach*, vol. I & II (D. Glover, ed.); *Oligonucleotide Synthesis* (N. Gait, ed., 1984); *Nucleic Acid Hybridization* (B. Hames & S. Higgins, eds., 1985); *Transcription and Translation* (B. Hames & S. Higgins, eds., 1984); *Animal Cell Culture* (R. Freshney, ed., 1986); Perbal, *A Practical Guide to Molecular Cloning* (1984).

All publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-

expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising epitopes, i.e., antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In specific embodiments, the polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

The polypeptides of the present invention are sometimes herein referred to as prostate-specific proteins or prostate-specific polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in prostate tissue samples. Thus, a "prostate-specific polypeptide" or "prostate-specific protein," refers generally to a polypeptide sequence of the present invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed

in a substantial proportion of prostate tissue samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of prostate tissue samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in other
5 normal tissues, as determined using a representative assay provided herein. A prostate-specific polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are
10 immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with prostate cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory*
15 *Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

20 As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide.
25 Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they
30 specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other

immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain has been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide composition set forth herein, such as those set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequence set forth herein.

In one preferred embodiment, the polypeptide fragments and variants provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of

the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader
5 sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another
10 amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide
15 with desirable characteristics, *e.g.*, with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

20 For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence
25 substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its

hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5);
5 glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are
10 within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of
15 its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 \pm 1); glutamate (+3.0 \pm 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5 \pm 1); alanine (−0.5); histidine (−0.5); cysteine
20 (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ± 2
25 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that
30 take various of the foregoing characteristics into consideration are well known to those

of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of
5 flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

10 Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values
15 include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a
20 preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

25 As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For
30 example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be “identical” if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

- Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

- Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known

tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al.,

Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to
5 separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and
10 transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus,
15 tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression
20 and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent
25 and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also*, Skeiky et al., *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the
30 purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous

immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine

amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been
5 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at
10 residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention,
15 when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4⁺ T-cells specific for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further
20 described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a
25 growing amino acid chain. *See Merrifield, J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of
30 the invention are isolated. An "isolated" polypeptide is one that is removed from its

original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99%
5 pure.

Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total
10 genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude
15 genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may
20 be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-
25 to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably an immunogenic variant or derivative, of such a sequence.

5 Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In certain preferred
10 embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

 In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this
25 invention using the methods described herein, (*e.g.*, BLAST analysis using standard
30

parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

5 Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous
10 genes of xenogenic origin.

In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to, or complementary to, one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at
15 least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103,
20 *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary
25 sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for
30 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in

the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, preferably 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent

sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present

invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25

nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single
5 stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

10 In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded
15 vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected
20 which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be
25 obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable
5 signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known
10 rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

15 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

20 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 contiguous nucleotides that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence
25 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a
30 sequence of interest will enable them to be of use in detecting the presence of

complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of
5 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in
10 various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger
15 contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in
20 length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

25 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various

factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCRTM technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, *e.g.*, one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to

destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention, 5 polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis 10 is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, 15 striatal GABA_A receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a 20 variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a 25 complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In 30 each case, preferred compositions comprise a sequence region that is complementary,

and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure, T_m ,
5 binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary
10 to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997 Sep 1;25(17):3389-402).

The use of an antisense delivery method employing a short peptide
15 vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered
20 into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme
25 molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For
30 example, a large number of ribozymes accelerate phosphoester transfer reactions with a

high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement
5 that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general,
10 enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to
15 cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many
20 technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of
25 target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action
30 (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the

specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis δ virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis δ virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO

92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes

expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*,

Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will
5 depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed
10 by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that
15 contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and
20 utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*,
25 Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to
30 therapeutics.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

Polynucleotide Identification, Characterization and Expression

Polynucleotide compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

reference in its entirety. Briefly, in PCRTM, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present
5 in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse
10 transcription and PCRTM amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCRTM amplification technique, are readily known and available in
15 the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat.
20 Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded
25 RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara,
30 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (*e.g.*, a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification.

- 5 Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

- For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can then be assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

- Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of

amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1*:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res. 19*:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (*e.g.*, Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be

confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

5 In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing
10 sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York.
15 N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid,
20 or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

25 The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription
30 and translation elements, including constitutive and inducible promoters, may be used.

For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses
5 are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example,
10 when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with
15 sequences for the amino-terminal Met and the subsequent 7 residues of β -galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are
20 soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

25 In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of
30 sequences encoding polypeptides may be driven by any of a number of promoters. For

example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of

skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

5 A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal
10 antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; *Serological Methods, a Laboratory Manual*, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

15 A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR
20 amplification using a labeled nucleotide. Alternatively, the sequences, or any portions thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used
25 include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained
30 intracellularly depending on the sequence and/or the vector used. As will be understood

by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant
5 or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

10 Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant (K_d) of the interaction, wherein a smaller K_d represents a greater
15 affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both
20 the "on rate constant" (K_{on}) and the "off rate constant" (K_{off}) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of K_{off}/K_{on} enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant K_d . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

25 An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable
30 regions" which are interposed between more conserved flanking stretches known as

"framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent.

For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation

of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab)₂" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V_H::V_L heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V_H::V_L heterodimer which is expressed from a gene fusion including V_H- and V_L-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an

antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (*e.g.*, a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRs. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) *Nature* 349:293-299; Lobuglio et al. (1989) *Proc. Nat. Acad. Sci. USA* 86:4220-4224; Shaw et al. (1987) *J Immunol.* 138:4534-4538; and Brown et al. (1987) *Cancer Res.* 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) *Nature* 332:323-327; Verhoeven et al. (1988) *Science* 239:1534-1536; and Jones et al. (1986) *Nature* 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) *Ann. Rev. Biochem.* 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (*e.g.*, electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in

this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the

intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by
5 serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody.
10 Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent
15 bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for
20 radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For
25 example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells

may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et

al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as

described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve

the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (*e.g.*, U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, *e.g.*, U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines* 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129;

Kotin, R. M. (1994) *Human Gene Therapy* 5:793-801; Shelling and Smith (1994) *Gene Therapy* 1:165-169; and Zhou et al. (1994) *J. Exp. Med.* 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, *Proc. Natl. Acad. Sci. USA* (1990) 87:6743-6747; Fuerst et al. *Proc. Natl. Acad. Sci. USA* (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer

protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant
5 Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, *e.g.*, WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in
10 U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et
15 al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner
20 et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al.,
25 *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in a specific location and orientation *via* homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the
30 polynucleotide may be stably maintained in the cell as a separate, episomal segment of

DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression
5 construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable
10 beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK)
15 and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device,
20 propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639
25 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances
30 or potentiates an immune response (antibody and/or cell-mediated) to an exogenous

antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins.

5 Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated

10 sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Within certain embodiments of the invention, the adjuvant composition

15 is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as

20 provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman,

25 *Ann. Rev. Immunol.* 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL[®] adjuvants are available from Corixa Corporation (Seattle, WA; see, for example, US

30 Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing

oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by
5 Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example
10 combinations of at least two of the following group comprising QS21, QS7, Quil A, β -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix,
15 particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or
20 suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol^R to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

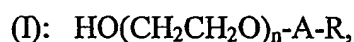
In one preferred embodiment, the adjuvant system includes the
25 combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL[®] adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-

MPL[®] adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn[®]; Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



wherein, n is 1-50, A is a bond or $-\text{C}(\text{O})-$, R is C_{1-50} alkyl or Phenyl C_{1-50} alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein n is between 1 and 50, preferably 4-24, most preferably 9; the R component is C_{1-50} , preferably $\text{C}_4\text{-C}_{20}$ alkyl and most preferably C_{12} alkyl, and A is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12th edition: entry 7717). These adjuvant molecules are described in WO

99/52549. The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

5 According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or
10 maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

15 Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In
20 general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex*
25 *vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

 Dendritic cells and progenitors may be obtained from peripheral blood,
30 bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph

nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from
5 peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature"
10 cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature
15 phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the
20 invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be
25 administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or
30 progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release. In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763;

5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they

may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared in such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

For oral administration, the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or

by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride.

- 5 Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered
10 isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml
15 of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity
20 standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for
25 example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be

administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption
5 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase
10 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the
15 lungs *via* nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of
20 a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid
25 particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example,
30 Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998

Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

5 Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery
10 systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

15 In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

 Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the
20 present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μ m) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for
25 example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of prostate cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g., intracutaneous,*

intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)

obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and polypeptide portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized

on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed

and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10

nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the

cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound
5 binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific
10 for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

15 The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein.
20 Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

25 Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be

present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from
10 prostate tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA
15 was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns
20 (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA
25 libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69% of clones
30 having inserts and the average insert size being 1120 base pairs. For both libraries,

sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor
5 and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol
10 precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the
15 DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of
20 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three
25 more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E.*

coli DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 μ g each of human glandular kallikrein, PSA and

mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

5 Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA
10 sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively).
15 Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike,
20 four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant
25 homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding

predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807,

1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the
5 isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were
10 over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-
15 4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively,
20 and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297,
25 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-

4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

The determined cDNA sequences for additional prostate-specific clones isolated during characterization of prostate specific cDNA libraries are provided in SEQ ID NO: 618-689, 691-697 and 709-772. Comparison of these sequences with those in the public databases revealed no significant homologies to any of these sequences.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

5 Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

10 Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was
15 used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for
20 each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

 mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung
25 tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at
30 high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon

and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney,

ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. Subsequent comparison of the sequence of SEQ ID NO: 384 with sequences in the public databases, led to the identification of a full-length cDNA sequence of P1000C (SEQ ID NO: 929), which encodes a 492 amino acid sequence.

Analysis of the amino acid sequence using the PSORT II program led to the identification of a putative transmembrane domain from amino acids 84-100. The cDNA sequence of the open reading frame of P1000C, including the stop codon, is provided in SEQ ID NO: 930, with the open reading frame without the stop codon being
5 provided in SEQ ID NO: 931. The full-length amino acid sequence of P1000C is provided in SEQ ID NO: 932. SEQ ID NO: 933 and 934 represent amino acids 1-100 and 100-492 of P1000C, respectively.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by
10 immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

15 The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver,
20 brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that
25 this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC
POLYPEPTIDES BY PCR-BASED SUBTRACTION

5 A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The
10 resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF⁺ *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA
15 sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID
20 NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences
25 which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 699-701.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA
30 sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145,

147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones
5 containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is
10 provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine
15 and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed
20 comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor
25 compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal
30 prostate and prostate tumor, compared to six of twelve other normal tissues tested.

Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and
5 normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-
10 h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in
15 the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

20 mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor
25 and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both microarray technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those
5 in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

10 PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in
15 SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of
20 the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

Using computer algorithms, the following regions of P703P were predicted to represent potential HLA A2-binding CTL epitopes: amino acids 164-172
25 of SEQ ID NO: 525 (SEQ ID NO: 866); amino acids 160-168 of SEQ ID NO: 525 (SEQ ID NO: 867); amino acids 239-247 of SEQ ID NO: 525 (SEQ ID NO: 868); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 869); amino acids 112-120 of SEQ ID NO: 525 (SEQ ID NO: 870); amino acids 155-164 of SEQ ID NO: 525 (SEQ ID NO: 871); amino acids 117-126 of SEQ ID NO: 525 (SEQ ID NO: 872); amino acids
30 164-173 of SEQ ID NO: 525 (SEQ ID NO: 873); amino acids 154-163 of SEQ ID NO:

525 (SEQ ID NO: 874); amino acids 163-172 of SEQ ID NO: 525 (SEQ ID NO: 875); amino acids 58-66 of SEQ ID NO: 525 (SEQ ID NO: 876); and amino acids 59-67 of SEQ ID NO: 525 (SEQ ID NO: 877).

P703P was found to show some homology to previously identified proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor inhibit thrombin receptor activation and thrombin-induced platelet activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. The potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell membrane to promote tumorigenesis or activate a protease-activated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the P703P-receptor interaction may therefore be usefully employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of P703P expression increased with increasing Gleason score, indicating that P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are

provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P

were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 698. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

5 Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

10 Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an
15 ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on
20 chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential
25 open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The
30 full-length sequences for the two forms are provided in SEQ ID NO: 773 and 774, with

the corresponding amino acid sequences being provided in SEQ ID NO: 775 and 776, respectively. The cDNA sequence of SEQ ID NO: 774 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 776). This insert is not present in the sequence of SEQ ID NO: 773.

5 Further studies on P768P (SEQ ID NO: 315) led to the identification of the putative full-length open reading frame (ORF). The cDNA sequence of the ORF with stop codon is provided in SEQ ID NO: 907. The cDNA sequence of the ORF without stop codon is provided in SEQ ID NO: 908, with the corresponding amino acid sequence being provided in SEQ ID NO: 909. This sequence was found to show 86%
10 identity to a rat calcium transporter protein, indicating that P768P may represent a human calcium transporter protein. The locations of transmembrane domains within P768P were predicted using the PSORT II computer algorithm. Six transmembrane domains were predicted at amino acid positions 118-134, 172-188, 211-227, 230-246, 282-298 and 348-364. The amino acid sequences of SEQ ID NO: 910-915 represent
15 amino acids 1-134, 135-188, 189-227, 228-246, 247-298 and 299-511 of P768P, respectively.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

20 Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of
25 conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid
30 (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of

0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

5

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

10 A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide
15 restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

20 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate
25 hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences
30 which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich
5 differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

10 In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for
15 proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA
20 sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant
25 homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most
30 prostate tumors and BPH tissues by a factor of three or greater, with elevated expression

seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

5 Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349,
10 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant
15 homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is
20 shown in Figure 12A (SEQ ID NO: 777), with the corresponding predicted amino acid being shown in Figure 12B (SEQ ID NO: 778). Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 779, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this
25 polymorphic variant of P788P is provided in SEQ ID NO: 779, with the corresponding amino acid sequence being provided in SEQ ID NO: 780. The sequence of SEQ ID NO: 780 differs from that of SEQ ID NO: 778 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively. Further studies led to the isolation of the full-length sequence for the clone of SEQ ID NO: 570 (provided in SEQ ID NO: 880). Full-length cloning efforts on the clone of SEQ ID NO: 571 led to the isolation of two sequences (provided in SEQ ID NO: 881 and 882), representing a single clone, that are identical with the exception of a polymorphic insertion/deletion at position 1293. Specifically, the clone of SEQ ID NO: 882 (referred to as clone F1) has a C at position 1293. The clone of SEQ ID NO: 881 (referred to as clone F2) has a single base pair deletion at position 1293. The predicted amino acid sequences encoded by 5 open reading frames located within SEQ ID NO: 880 are provided in SEQ ID NO: 883-887, with the predicted amino acid sequences encoded by the clone of SEQ ID NO: 881 and 882 being provided in SEQ ID NO: 888-893.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common,

suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

- 5 The clone of SEQ ID NO: 342 (referred to as P789P) was found to show homology to a previously identified gene. The full length cDNA sequence for P789P and the corresponding amino acid sequence are provided in SEQ ID NO: 878 and 879, respectively.

10

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

- 15 Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were
20 immunized with 100 μ g of P2S#12 and 120 μ g of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium
25 pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 μ g/ml dextran sulfate and 25 μ g/ml LPS for 3 days). Six days later, cells (5×10^5 /ml) were
30 restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells

(Sherman et al, *Science* 258:815-818, 1992) and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed
5 EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with
10 P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

15 6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is
20 derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding
25 using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 μ g/ml were added to
30 cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes,

CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

5 Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 μ g of P1S #10 and 120 μ g of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single
10 cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6×10^6 cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2 μ g/ml P1S#10 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 μ g/ml dextran sulfate and 25 μ g/ml LPS for 3 days). Six days later cells (5×10^5 /ml) were restimulated
15 with 2.5×10^6 /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as
20 shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were
25 isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION

WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred
5 to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research
Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012
either intramuscularly or intradermally. The mice were immunized three times, with a
two week interval between immunizations. Two weeks after the last immunization,
immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator
10 cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL
activity was assessed against P501S transduced targets. Two out of 8 mice developed
strong anti-P501S CTL responses. These results demonstrate that P501S contains at
least one naturally processed HLA-A2-restricted CTL epitope.

15

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate
tumor polypeptide to recognize human tumor.

20 Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ
ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells
according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75,
1998). The resulting CD8⁺ T cell microcultures were tested for their ability to
recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which
25 were transduced to express the P502S gene in a γ-interferon ELISPOT assay (*see*
Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells
were assayed in duplicate on 10⁴ fibroblasts in the presence of 3 µg/ml human β₂-
microglobulin and 1 µg/ml P2S-12 peptide or control E75 peptide. In addition, T cells
were simultaneously assayed on autologous fibroblasts transduced with the P502S gene
30 or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the

fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

20

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts

retrovirally transduced to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (^{51}Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997*). The results of these assays are presented in Figures 6A and 6B.

10

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN THE
PROSTATE-SPECIFIC ANTIGEN P703P

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 μg of p5 peptide together with 140 μg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the

control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte
5 cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures,
10 CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being
15 recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 781, with the corresponding cDNA sequence being provided in SEQ ID NO: 782.

Twenty 15-mer peptides overlapping by 10 amino acids and derived
20 from the carboxy-terminal fragment of P703P were generated using standard procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration
25 of 0.25 microgram/ml. Pulsed DC were washed and plated at 1×10^4 cells/well of 96-well V-bottom plates and purified CD4 T cells were added at 1×10^5 /well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2.
30 Following 4 *in vitro* stimulation cycles, 96 lines (each line corresponding to one well) were tested for specific proliferation and cytokine production in response to the

stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by ³H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 781). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVS VVS (SEQ ID NO: 781) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of

recombinant P703P sources were utilized; *E. coli*-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were *E. coli*-derived L3E (a lung-specific antigen) and baculovirus-derived mammaglobin. In interferon-gamma ELISA assays, line 1-F9 was able to efficiently recognize both *E. coli* forms of P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the *E. coli* and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) from P703P is a naturally processed peptide epitope derived from P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are provided in SEQ ID NO: 799-814, with the corresponding cDNA sequences being provided in SEQ ID NO: 783-798, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cells lines were restimulated on the

appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in *E. coli* (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in *E. coli*. Of the T cell lines tested, line I-1A
5 recognized specifically the truncated form of P703P (*E. coli*) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (*E. coli*) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or
10 were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDLMLIKLDE (SEQ ID NO: 814; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A, and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 811; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 810; corresponding to a.a. 135-149 of
15 SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

In further studies, forty 15-mer peptides overlapping by 10 amino acids and derived spanning amino acids 47 to 254 of P703P (SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was
20 determined essentially as described above. DC were prepared from PBMC of a donor having distinct HLA DR and DQ alleles from that used in previous experiments. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 0.25 microgram/ml, and each pool containing 10 peptides. Twelve lines were identified that demonstrated specific proliferation and cytokine production
25 (measured in gamma-interferon ELISA assays) in response to the stimulating peptide pool. These lines were further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and specific recognition of recombinant P703P protein. Lines 3A5H and 3A9H specifically proliferated and produced gamma-interferon in response to recombinant protein and one individual
30 peptide as well as the peptide pool. Following re-stimulation on targets loaded with the specific peptide, only 3A9H responded specifically to targets exposed to lysates of

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fibroblasts infected adenovirus expressing full-length P703P. These results indicates that the line 3A9H can respond to antigenic peptide derived from protein synthesized in mammalian cells. The peptide to which the specific CD4 line responded correspond to amino acids 155-170 of P703P (SEQ ID NO: 943). The DNA sequence for this peptide
5 is provided in SEQ ID NO: 942.

EXAMPLE 11

EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

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Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino
15 acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is
20 provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that
25 B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing

Gleason grade, demonstrating that expression of B305D increases as prostate cancer progresses.

EXAMPLE 12

5 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996),
10 human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte
15 cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+
20 T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous
25 fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8⁺ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also

transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percol gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501S-expressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a γ -IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and
5 CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL, pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid sequence of P501S were loaded onto autologous B-LCL and tested in γ -IFN Elispot assays for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5
10 and 4E7. One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer peptides that comprised the positive pool were tested individually in γ -IFN Elispot assays for the ability to stimulate the two P501S-specific CTL clones, 4E5 and
15 4E7. Both 4E5 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 853; cDNA sequence provided in SEQ ID NO: 854) that spanned amino acids 453-472 of P501S. Since the minimal epitope recognized by CD8+ T cells is almost always either a 9 or 10-mer peptide sequence, 10-mer peptides that spanned the entire sequence of SEQ ID NO: 853 were synthesized that differed by 1 amino acid. Each of these 10-mer
20 peptides was tested for the ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer peptide (SEQ ID NO: 855; cDNA sequence provided in SEQ ID NO: 856) was identified that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-472 of P501S. This sequence defines a minimal 10-mer epitope from P501S that can be naturally processed and to which CTL responses
25 can be identified in normal PBMC. Thus, this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of SEQ ID NO: 855, HLA blocking and mismatch analyses were performed. In γ -IFN Elispot assays, the specific response of clones 4A7 and 4E5 to P501S-transduced
30 autologous fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking antibody) and B1.23.2 (HLA-B/C blocking antibody). These results

demonstrate that the SEQ ID NO: 855-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, autologous B-LCL (HLA-A1,A2,B8,B51, Cw1, Cw7) and heterologous B-LCL (HLA-A2,A3,B18,B51,Cw5,Cw14) that share the HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 855, washed, and tested in γ -IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5. Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 855-specific response was detected using both the autologous (D326) and heterologous (D107) B-LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 855 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 855, two 9-mers with the sequences of SEQ ID NO: 857 and 858 were synthesized and tested in Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 855, as well as the 9-mer peptide of SEQ ID NO: 858, but not the 9-mer peptide of SEQ ID NO: 857, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 858 is a 9-mer P501S-derived epitope recognized by P501S-specific CTL. The DNA sequence encoding the epitope of SEQ ID NO: 858 is provided in SEQ ID NO: 859.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 855 and 858 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and co-transfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of

stimulating the P501S-specific CTL to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the
5 subtype of the relevant restricting allele is HLA-B51011.

To determine if the P501S-specific CTL could recognize prostate tumor cells that express P501S, the P501S-positive lines LnCAP and CRL2422 (both expressing "moderate" amounts of P501S mRNA and protein), and PC-3 (expressing low amounts of P501S mRNA and protein), plus the P501S-negative cell line DU-145
10 were retrovirally transduced with the HLA-B51011 allele that was cloned from the donor used to generate the P501S-specific CTL. HLA-B51011- or EGFP-transduced and selected tumor cells were treated with gamma-interferon and androgen (to upregulate stimulatory functions and P501S, respectively) and used in gamma-interferon Elispot assays with the P501S-specific CTL clones 4E5 and 4E7. Untreated
15 cells were used as a control.

Both 4E5 and 4E7 efficiently and specifically recognized LnCAP and CRL2422 cells that were transduced with the HLA-B51011 allele, but not the same cell lines transduced with EGFP. Additionally, both CTL clones specifically recognized PC-3 cells transduced with HLA-B51011, but not the P501S-negative tumor cell line
20 DU-145. Treatment with gamma-interferon or androgen did not enhance the ability of CTL to recognize tumor cells. These results demonstrate that P501S-specific CTL, generated by *in vitro* whole gene priming, specifically and efficiently recognize prostate tumor cell lines that express P501S.

A naturally processed CD4 epitope of P501S was identified as follows.

25 CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1- 325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 µg/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed
30 with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4

stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using γ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4 μ g/ml or an irrelevant peptide at μ g/ml were used as APC. T cell lines that demonstrated either
5 specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

From pool A, lines AD9 and AE10 specifically recognized peptide 1 (SEQ ID NO: 862), and line AF5 recognized peptide 39 (SEQ ID NO: 861). From pool
10 B, line BC6 could be identified that recognized peptide 58 (SEQ ID NO: 860). Each of these lines were stimulated on the specific peptide and tested for specific recognition of the peptide in a titration assay as well as cell lysates generated by infection of HEK 293 cells with adenovirus expressing either P501S or an irrelevant antigen. For these assays, APC-adherent monocytes were pulsed with either 10, 1, or 0.1 μ g/ml individual P501S
15 peptides, and DC were pulsed overnight with a 1:5 dilution of adenovirally infected cell lysates. Lines AD9, AE10 and AF5 retained significant recognition of the relevant P501S-derived peptides even at 0.1 mg/ml. Furthermore, line AD9 demonstrated significant (8.1 fold stimulation index) specific activity for lysates from adenovirus-P501S infected cells. These results demonstrate that high affinity CD4 T cell lines can
20 be generated toward P501S-derived epitopes, and that at least a subset of these T cells specific for the P501S derived sequence of SEQ ID NO: 862 are specific for an epitope that is naturally processed by human cells. The DNA sequences encoding the amino acid sequences of SEQ ID NO: 860-862 are provided in SEQ ID NO: 863-865, respectively.

25 To further characterize the P501S-specific activity of AD9, the line was cloned using anti-CD3. Three clones, referred to as 1A1, 1A9 and 1F5, were identified that were specific for the P501S-1 peptide (SEQ ID NO: 862). To determine the HLA restriction allele for the P501S-specific response, each of these clones was tested in class II antibody blocking and HLA mismatch assays using proliferation and gamma-
30 interferon assays. In antibody blocking assays and measuring gamma-interferon production using ELISA assays, the ability of all three clones to recognize peptide

pulsed APC was specifically blocked by co-incubation with either a pan-class II blocking antibody or a HLA-DR blocking antibody, but not with a HLA-DQ or an irrelevant antibody. Proliferation assays performed simultaneously with the same cells confirmed these results. These data indicate that the P501S-specific response of the clones is restricted by an HLA-DR allele. Further studies demonstrated that the restricting allele for the P501S-specific response is HLA-DRB1501.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table ISummary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other

normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 702-705. An amino acid sequence encoded by SEQ ID NO: 705 is provided in SEQ ID NO: 706. The cDNA sequence of SEQ ID NO: 702 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 707 and 708.

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatazizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II
Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

5 Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the

10 Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters

15 (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table IIIProstate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

5 The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

15 Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that
5 encodes the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

EXAMPLE 15

10 FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above
15 was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-460 represent novel genes. The others (SEQ ID NO: 454-
20 458 and 461-467) correspond to known sequences. Comparison of the determined

cDNA sequence of SEQ ID NO: 461 with sequences in the Genbank database using the BLAST program revealed homology to the previously identified transmembrane protease serine 2 (TMPRSS2). The full-length cDNA sequence for this clone is provided in SEQ ID NO: 894, with the corresponding amino acid sequence being
5 provided in SEQ ID NO: 895. The cDNA sequence encoding the first 209 amino acids of TMPRSS2 is provided in SEQ ID NO: 896, with the first 209 amino acids being provided in SEQ ID NO: 897.

The sequence of SEQ ID NO: 462 (referred to as P835P) was found to correspond to the previously identified clone FLJ13518 (Accession AK023643; SEQ ID
10 NO: 917), which had no associated open reading frame (ORF). This clone was used to search the Geneseq DNA database and matched a clone previously identified as a G protein-coupled receptor protein (DNA Geneseq Accession A09351; amino acid Geneseq Accession Y92365), that is characterized by the presence of seven transmembrane domains. The sequences of fragments between these domains are
15 provided in SEQ ID NO: 921-928, with SEQ ID NO: 921, 923, 925 and 927 representing extracellular domains and SEQ ID NO: 922, 924, 926 and 928 representing intracellular domains. SEQ ID NO: 921-928 represent amino acids 1-28, 53-61, 83-103, 124-143, 165-201, 226-238, 263-272 and 297-381, respectively, of P835P. The full-length cDNA sequence for P835P is provided in SEQ ID NO: 916. The cDNA
20 sequence of the open reading frame for P835P, including stop codon, is provided in SEQ ID NO: 918, with the open reading frame without stop codon being provided in SEQ ID NO: 919 and the corresponding amino acid sequence being provided in SEQ ID NO: 920.

25

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P
30 fragment described above. One million colonies were plated on LB/Ampicillin plates.

Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 690.

EXAMPLE 17

PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostate-specific antigens in *E. coli*, baculovirus and mammalian cells.

a) Expression of P501S in *E. coli*

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was

cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The
5 resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression
10 was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen
15 Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as
20 Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to
25 aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of
30 the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S

DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The
5 sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C
10 fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 848) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 849) and AW053 (SEQ ID NO: 850). AW042 is a sense
15 cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein
20 was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM β -Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 851 and 852, respectfully.

25 b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the

manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553 amino acids; SEQ ID NO: 113) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The

Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

d) Expression of P703P in Baculovirus

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein:

e) Expression of P788P in *E. Coli*

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in *E. coli* as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 815 and 816). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the designed construct. The expression construct P788P-N #6/pCRX1 was transformed into *E. coli* BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD600 of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 817, with the corresponding amino acid sequence being provided in SEQ ID NO: 818.

f) Expression of P510S in *E. coli*

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in *E. coli* as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal end, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 820 and 821, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and

vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A mini-induction screen was performed to optimize the expression conditions. After induction
5 the cells grew well, achieving OD 600 nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin +
10 chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 822 and 825,
15 respectively.

The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to that used for Ra12-P510S-C, except that the PCR primers
20 employed were those shown in SEQ ID NO: 828 and 829, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 828 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 829 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3)
25 CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein sequencing. The optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (+
30 kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow

to grow at 37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-C construct are shown in SEQ ID NO: 823 and 826, respectively.

5 The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in *E. coli* as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 830 and 831. The primer of SEQ ID NO: 830 is a sense primer with an NdeI site for use in ligating into pPDM. The primer of SEQ ID NO: 831 is an antisense primer with an added XhoI site
10 for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing
15 confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3
20 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-E3 construct are provided in SEQ ID NO: 824 and 827, respectively.

g) Expression of P775S in *E. Coli*

25 The antigen P775P contains multiple open reading frames (ORF). The third ORF, encoding the protein of SEQ ID NO: 483, has the best motif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 832 and the anti-sense PCR primer of SEQ ID NO: 833. The PCR amplified fragment of P775P and

Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after
5 induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 834 and 835, respectively.

10

H) Expression of a P703P His tag fusion protein in *E. coli*

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 836 and 837. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag
15 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 838 and 839, respectively.

20

I) Expression of a P705P His tag fusion protein in *E. coli*

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 840 and 841. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag
25 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 842 and 843, respectively.

30

J) Expression of a P711P His tag fusion protein in *E. coli*

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 844 and 845. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 846 and 847, respectively.

K) Expression of P767P in *E. coli*

The full-length coding region of P767P (amino acids 2-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-468 and PDM-469 (SEQ ID NO: 935 and 936, respectively). DNA amplification was performed using 10 µl 10X Pfu buffer, 1 µl 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 66°C for 15 sec and by 72°C for 2 min., and lastly by 1 cycle of 72°C for 4 min. The PCR product was digested with XhoI and cloned into a modified pET28 vector with a histidine tag in frame on the 5' end that was digested with Eco72I and XhoI. The construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The cDNA coding region for the recombinant B767P protein is provided in SEQ ID NO: 938, with the corresponding amino acid sequence being provided in SEQ ID NO: 941. The full-length P767P did not express at high enough levels for detection or purification.

A truncated coding region of P767P (referred to as B767P-B; amino acids 47-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-573 and PDM-469 (SEQ ID NO: 937 and 936, respectively) and the PCR conditions described above for full-length P767P. The PCR product was digested with XhoI and cloned into the modified pET28 vector that was digested with Eco72I and XhoI. The

construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The protein was found to be expressed in the inclusion body pellet. The coding region for the expressed B767P-B protein is provided in SEQ ID NO: 939, with the corresponding amino acid sequence
5 being provided in SEQ ID NO: 940.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

10

a) Preparation and Characterization of Polyclonal Antibodies against P703P, P504S and P509S

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

15 Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml to 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were
20 induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run
25 through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed

inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then vialled after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyl dipeptide (MDP). Every four weeks rabbits were boosted with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250 microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 min. Plates were again

washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H₂SO₄ and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

b) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ($\mu\text{g/ml}$)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

- 5 The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 $\mu\text{g/ml}$, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using
- 10 an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-
- 15 LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described

above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-

mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors,

5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

c) Preparation and Characterization of Antibodies against P503S

5 A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at
10 Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur

fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

d) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM

technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk^{-/-} cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure

specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

e) Preparation and Characterization of Antibodies against P504S

Full-length P504S (SEQ ID NO: 108) was expressed and purified from bacteria essentially as described above for P501S and employed to raise rabbit monoclonal antibodies using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). The anti-P504S monoclonal antibody 13H4 was shown by Western blot to bind to both expressed recombinant P504S and to native P504S in tumor cells.

Immunohistochemical studies using 13H4 to assess P504S expression in various prostate tissues were performed as described above. A total of 104 cases, including 65 cases of radical prostatectomies with prostate cancer (PC), 26 cases of prostate biopsies and 13 cases of benign prostate hyperplasia (BPH), were stained with the anti-P504S monoclonal antibody 13H4. P504S showed strongly cytoplasmic granular staining in 64/65 (98.5%) of PCs in prostatectomies and 26/26 (100%) of PCs in prostatic biopsies. P504S was stained strongly and diffusely in carcinomas (4+ in 91.2% of cases of PC; 3+ in 5.5%; 2+ in 2.2% and 1+ in 1.1%) and high grade prostatic intraepithelial neoplasia (4+ in all cases). The expression of P504S did not vary with Gleason score. Only 17/91 (18.7%) of cases of NP/BPH around PC and 2/13 (15.4%) of BPH cases were focally (1+, no 2+ to 4+ in all cases) and weakly positive for P504S in large glands. Expression of P504S was not found in small atrophic glands, postatrophic hyperplasia, basal cell hyperplasia and transitional cell metaplasia in either biopsies or prostatectomies. P504S was thus found to be over-expressed in all Gleason scores of prostate cancer (98.5 to 100% of sensitivity) and exhibited only focal positivities in

large normal glands in 19/104 of cases (82.3% of specificity). These findings indicate that P504S may be usefully employed for the diagnosis of prostate cancer.

EXAMPLE 19

5 CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine
10 the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow
15 the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains.
20 Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

25 Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the
30 substitution of the histidine with an asparagine, was synthesized as described above. A

Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether.

- 5 The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described
- 10 above.

- Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell
- 15 sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and
- 20 stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (*i.e.*, intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

- 25 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun
- 30 at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C.

Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of

SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

In further studies, mouse monoclonal antibodies were raised against amino acids 296 to 322 to P501S, which are predicted to be in an extracellular domain. A/J mice were immunized with P501S/adenovirus, followed by subsequent boosts with an *E. coli* recombinant protein, referred to as P501N, that contains amino acids 296 to 322 of P501S, and with peptide 296-322 (SEQ ID NO: 898) coupled with KLH. The mice were subsequently used for splenic B cell fusions to generate anti-peptide hybridomas. The resulting 3 clones, referred to as 4F4 (IgG1,kappa), 4G5 (IgG2a,kappa) and 9B9 (IgG1,kappa), were grown for antibody production. The 4G5 mAb was purified by passing the supernatant over a Protein A-sepharose column,

followed by antibody elution using 0.2M glycine, pH 2.3. Purified antibody was neutralized by the addition of 1M Tris, pH 8, and buffer exchanged into PBS.

For ELISA analysis, 96 well plates were coated with P501S peptide 296-322 (referred to as P501-long), an irrelevant P775 peptide, P501S-N, P501TR2, P501S-long-KLH, P501S peptide 306-319 (referred to as P501-short)-KLH, or the irrelevant peptide 2073-KLH, all at a concentration of 2 ug/ml and allowed to incubate for 60 minutes at 37 °C. After coating, plates were washed 5X with PBS + 0.1% Tween and then blocked with PBS, 0.5% BSA, 0.4% Tween20 for 2 hours at room temperature. Following the addition of supernatants or purified mAb, the plates were incubated for 60 minutes at room temperature. Plates were washed as above and donkey anti-mouse IgHRP-linked secondary antibody was added and incubated for 30 minutes at room temperature, followed by a final washing as above. TMB peroxidase substrate was added and incubated 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1N H₂SO₄ and the OD was read at 450 nM. All three hybrid clones secreted mAb that recognized peptide 296-322 and the recombinant protein P501N.

For FACS analysis, HEK293 cells were transiently transfected with a P501S/VR1012 expression constructs using Fugene 6 reagent. After 2 days of culture, cells were harvested and washed, then incubated with purified 4G5 mAb for 30 minutes on ice. After several washes in PBS, 0.5% BSA, 0.01% azide, goat anti-mouse Ig-FITC was added to the cells and incubated for 30 minutes on ice. Cells were washed and resuspended in wash buffer including 1% propidium iodide and subjected to FACS analysis. The FACS analysis confirmed that amino acids 296-322 of P501S are in an extracellular domain and are cell surface expressed.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server

(<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al.* *Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

EXAMPLE 20

REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture system as follows.

15

Cells from the prostate tumor cell line LNCaP were plated at 1.5×10^6 cells/T75 flask (for RNA isolation) or 3×10^5 cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3-G4-D3 and permeabilized cells.

25

For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM Na_2HPO_4 , 70 mM H_3PO_4 , 1 mM EDTA, 1% SDS, 1% BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was

30

labeled with ^{32}P using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 0.001 M Na_2EDTA), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found to increase in response to androgen treatment.

10

EXAMPLE 21

PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids). The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP

cDNA was cloned into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ ID NO: 617.

5 The fusion FOPP was expressed as a single recombinant protein in *E. coli* as follows. The expression plasmid pCRX1FOPP was transformed into the *E. coli* strain BL21-CodonPlus RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml
10 chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the
15 cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl
20 pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing
25 FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at - 70 °C.

EXAMPLE 22

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN
PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

5 Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the TaqmanTM procedure using both gene specific primers and probes to determine the levels of gene expression.

10 Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0
15 and subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the TaqmanTM procedure but extending to 50 cycles using
20 forward and reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and β -actin signal. The remaining 2 samples had no detectable β -actin or P501S. No P501S signal was observed in the four normal blood samples tested.

25

EXAMPLE 23

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN
SCID MOUSE-PASSAGED PROSTATE TUMORS

30 When considering the effectiveness of antigens in the treatment of prostate cancer, the continued presence of the antigens in tumors during androgen

ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

Two prostate tumors that had metastasized to the bone were removed
5 from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and normal heart as negative controls. In both cases, the specific mRNA was
10 present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

EXAMPLE 24

15 ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH *IN VIVO*

The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

Ten SCID mice were injected subcutaneously with HEK293 cells that expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0
20 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

25

EXAMPLE 25

CHARACTERIZATION OF A T CELL RECEPTOR CLONE FROM A P501S-SPECIFIC T CELL CLONE

30 T cells have a limited lifespan. However, cloning of T cell receptor (TCR) chains and subsequent transfer essentially enables infinite propagation of the T

cell specificity. Cloning of tumor-antigen TCR chains allows the transfer of the specificity into T cells isolated from patients that share the TCR MHC-restricting allele. Such T cells could then be expanded and used in adoptive transfer settings to introduce the tumor antigen specificity into patients carrying tumors that express the antigen. T cell receptor alpha and beta chains from a CD8 T cell clone specific for the prostate-specific antigen P501S were isolated and sequenced as follows.

Total mRNA from 2×10^6 cells from CTL clone 4E5 (described above in Example 12) was isolated using Trizol reagent and cDNA was synthesized. To determine Va and Vb sequences in this clone, a panel of Va and Vb subtype-specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vb sequence that corresponded to the Vb7 subfamily. Furthermore, using cDNA generated from the clone, the Va sequence expressed was determined to be Va6. To clone the full TCR alpha and beta chains from clone 4E5, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows: TCR Valpha-6 5'(sense): GGATCC---GCCGCCACC---ATGTCACCTTTCTAGCCTGCT (SEQ ID NO: 899) BamHI site Kozak TCR alpha sequence TCR alpha 3' (antisense): GTCGAC---TCAGCTGGACCACAGCCGCAG (SEQ ID NO: 900) SalI site TCR alpha constant sequence TCR Vbeta-7. 5'(sense): GGATCC---GCCGCCACC---ATGGGCTGCAGGCTGCTCT (SEQ ID NO: 901) BamHI site Kozak TCR alpha sequence TCR beta 3' (antisense): GTCGAC---TCAGAAATCCTTTCTCTTGAC (SEQ ID NO: 902) SalI site TCR beta constant sequence. Standard 35 cycle RT-PCR reactions were established using cDNA synthesized from the CTL clone and the above primers, employing the proofreading thermostable polymerase PWO (Roche, Nutley, NJ).

The resultant specific bands (approx. 850 bp for alpha and approx. 950 for beta) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing full-length alpha and beta chains were identified, and large scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were submitted

for sequencing. The sequencing reactions demonstrated the cloning of full-length TCR alpha and beta chains with the determined cDNA sequences for the Vb and Va chains being shown in SEQ ID NO: 903 and 904, respectively. The corresponding amino acid sequences are shown in SEQ ID NO: 905 and 906, respectively. The Va sequence was shown by nucleotide sequence alignment to be 99% identical (347/348) to Va6.2, and the Vb to be 99% identical to Vb7 (336/338).

EXAMPLE 26

CAPTURE OF PROSTATE SPECIFIC CELLS USING

10 THE PROSTATE ANTIGEN P503S

As described above, P503S is found on the surface of prostate cells. Secondary coated microsphere beads specific for mouse IgG were coupled with the purified P503S-specific monoclonal antibody 1D12. The bound P503S antibody was then used to capture HEK cells expressing recombinant P503S. This provides a model system for prostate-specific cell capture which may be usefully employed in the detection of prostate cells in blood, and therefore in the detection of prostate cancer.

P503S-transfected HEK cells were harvested and redissolved in wash buffer (PBS, 0.1% BSA, 0.6% sodium citrate) at an appropriate volume to give at least 5^4 cells per sample. Round bottom Eppendorf tubes were used for all procedures involving beads. The stock concentrations were as shown below in Table VIII.

Table VIII

Stock concentrations	Sample concentration	Amount needed
Epithelial enrich beads 4^8 beads/ml (DynaL Biotech Inc. Lake Success, NY)	1^7 beads/ml	125 ul stock per 5 ml volume
1D12 ascites antibody 2 mg/ml	0.1 ug/ml (0.1X) to 5 ug/ml (5X) titrations	0.05 ul to 2.5 ul stock per sample
α - Mamma Mu 0.9 mg/ml	1 ug/ml (1X)	1.1 ul stock per sample
Pan-mouse IgG beads 4^8 beads/ml (DynaL Biotech)	1^7 beads/ml	125 ul stock per 5 ml volume

Blocked immunomagnetic beads were pre-washed as follows: all beads needed were pooled and washed once with 1 ml wash buffer. The beads were resuspended in a 3X volume of 1% BSA (v/v) in wash buffer and incubated for 15 min rotating at 4 °C. The beads were then washed three times with 2X volume of wash
5 buffer and resuspended to original volume. Non-blocked beads were pooled, washed three times with 2X volume of wash buffer and resuspended to original volume.

Primary antibody was incubated with secondary beads in a fresh Eppendorf for 30 minutes, rotating at 4 °C. Approximately 200 ul wash buffer was added to increase the total volume for even mixing of the sample. The antibody-bead
10 solution was transferred to a fresh Eppendorf, washed twice with an equal volume of wash buffer and resuspended to original volume. Target cells were added to each sample and incubated for 45 minutes, rotating at 4 °C. The tubes were transferred to a magnet, the supernatant removed, taking care not to agitate the beads, and the samples were washed twice with 1 ml wash buffer. The samples were then ready for RT-PCR
15 using a Dynabeads mRNA direct microkit (Dynal Biotech).

Epithelial cell enrichment was placed in a magnet and supernatant was removed. The epithelial enrichment beads were then resuspended in 100 ul lysis/binding buffer fortified with Rnasin (2 U/ul per sample), and stored at -70 °C until use. Oligo (dT₂₅) Dynabeads were pre-washed as follows: all beads needed were pooled (23
20 ul/sample), washed three times with an excess volume of lysis/binding buffer, and resuspended to original volume. The lysis supernatant was separated with a magnet and transferred to a fresh Eppendorf. 20 ul oligo(dT₂₅) Dynabeads were added per sample and rolled for 5 min at room temperature. Supernatant was separated using a magnet and discarded, leaving the mRNA annealed to the beads. The bead/mRNA
25 complex was washed with buffer and resuspended in cold Tris-HCl.

For RT-PCR, the Tris-HCl supernatant was separated and discarded using MPS. For each sample containing 1⁵ cells or less, the following was added to give a total volume of 30 ul: 14.25 ul H₂O; 1.5 ul BSA; 6 ul first strand buffer; 0.75 mL 10 mM dNTP mix; 3 ul Rnasin; 3 ul 0.1M dTT; and 1.5 ul Superscript II. The resulting
30 solution was incubated for 1 hour at 42 °C, diluted 1:5 in H₂O, heated at 80°C for 2 min

to detach cDNA from the beads, and immediately placed on MPS. The supernatant containing cDNA was transferred to a new tube and stored at -20°C .

Table IX shows the percentage of capture of P503S-transfected HEK cells as determined by RT-PCR.

5

Table IX

	% capture P503S-transfected HEK cells	% capture LnCAP cells
0.1 ug/ml P503S Mab	36.90	0.00
0.5 ug/ml P503S Mab	67.40	2.93
1 ug/ml P503S Mab	40.22	0.00
5 ug/ml P503S Mab	13.11	0.00
Anti-Mu beads only, non-blocked	1.42	0.00
Anti-Mu beads only, blocked	15.65	20.21
Absolute control, non-capture cells	100.00	100.00

10

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(b) sequences having at least 70% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(c) sequences having at least 90% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(d) sequences encoded by a polynucleotide of claim 1;

(e) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(f) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;

(c) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591,

593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 2,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

13. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

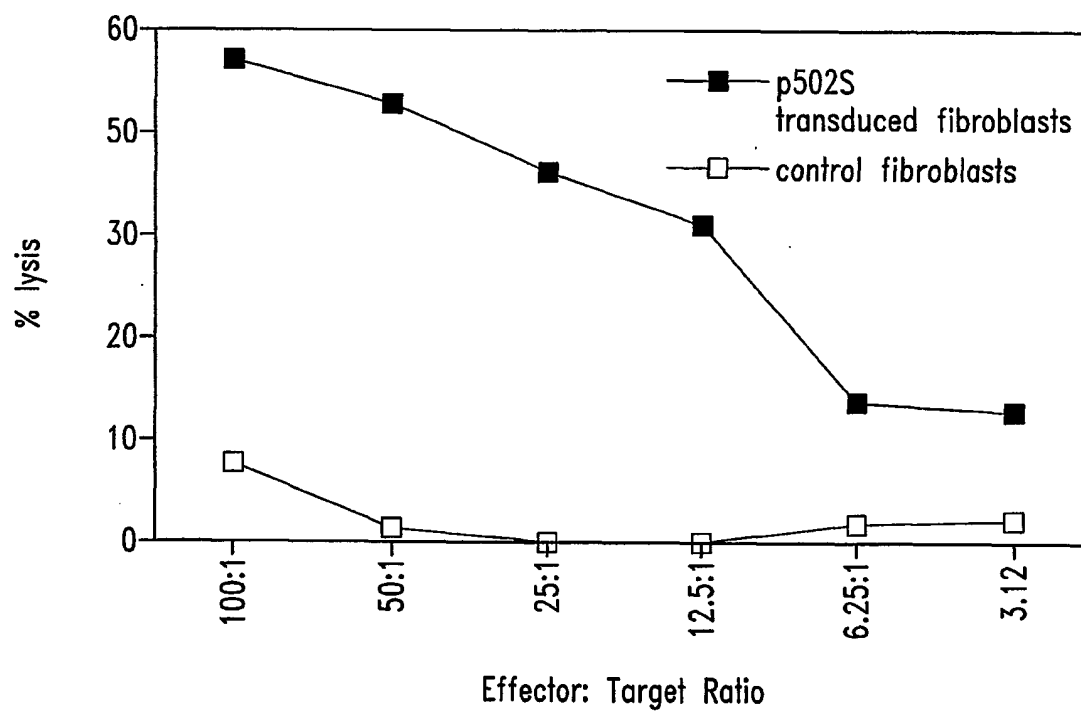
16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

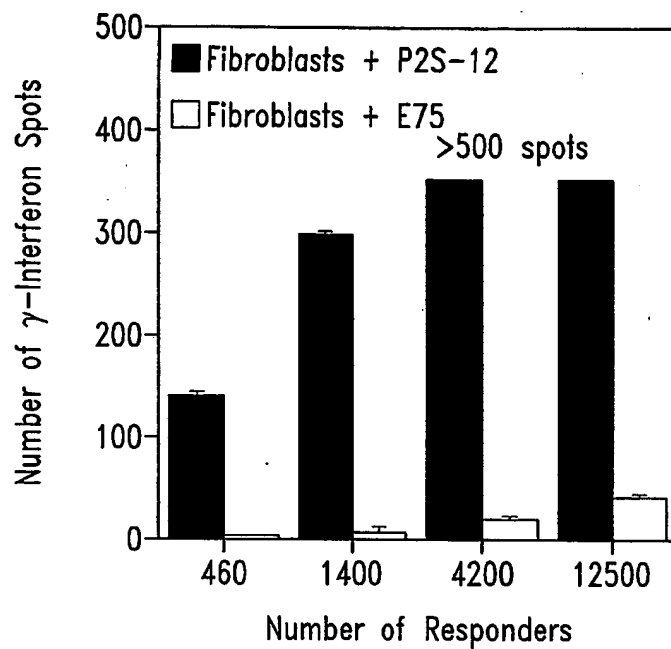
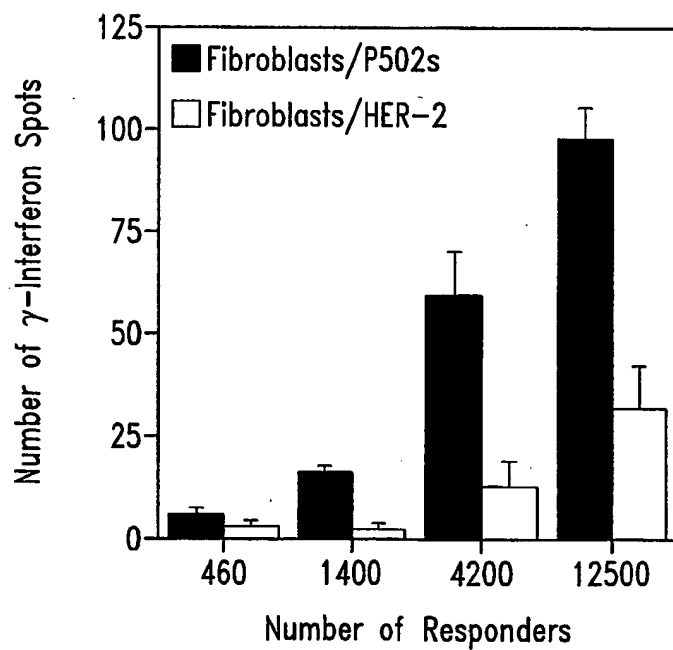
- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;
- (b) administering to the patient an effective amount of the proliferated T cells,

and thereby inhibiting the development of a cancer in the patient.

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*Fig. 1*

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*Fig. 2A**Fig. 2B*

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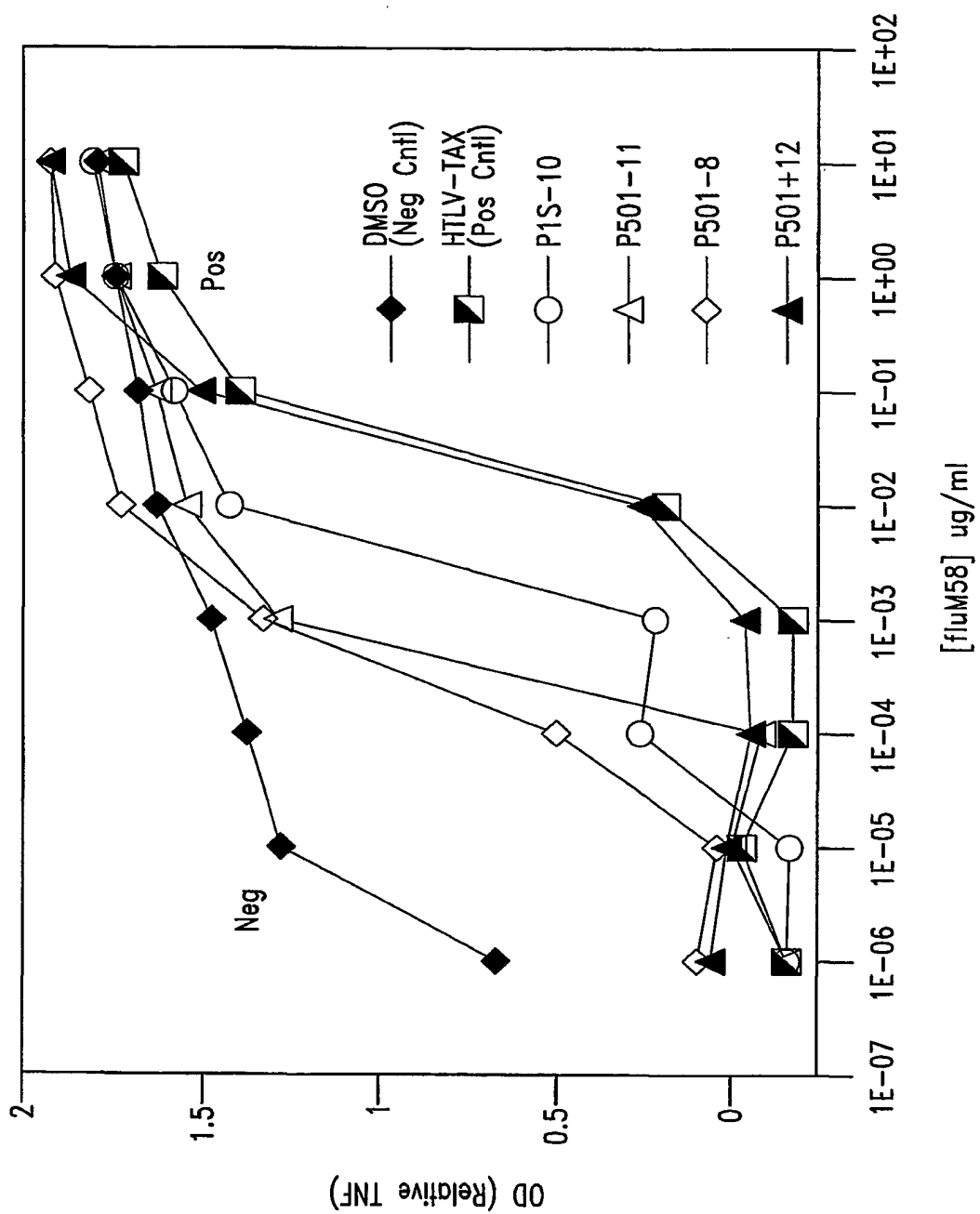
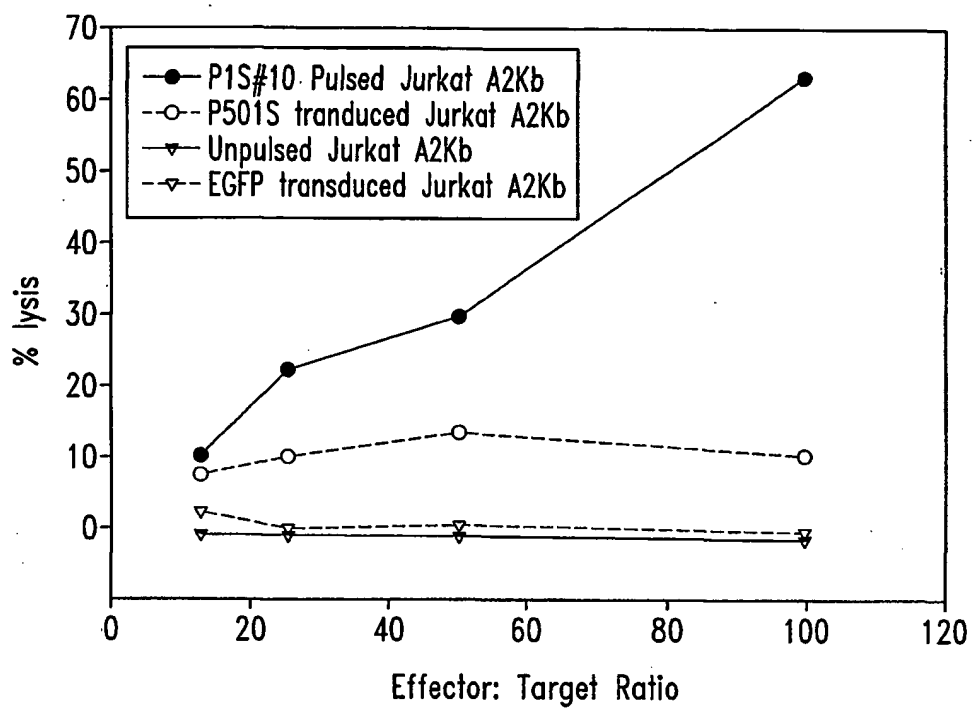
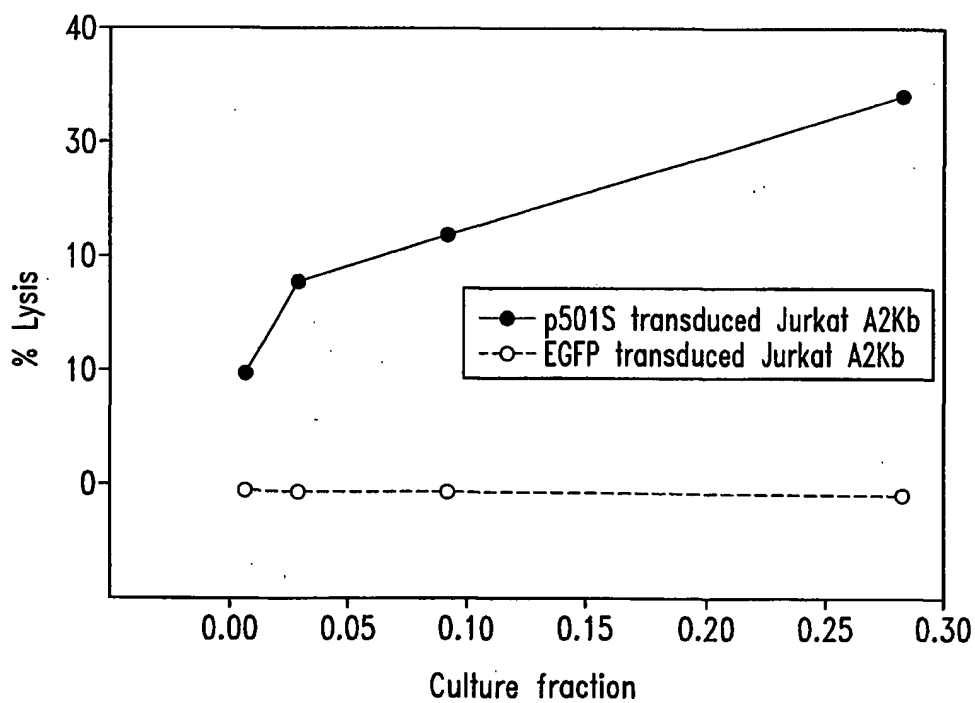
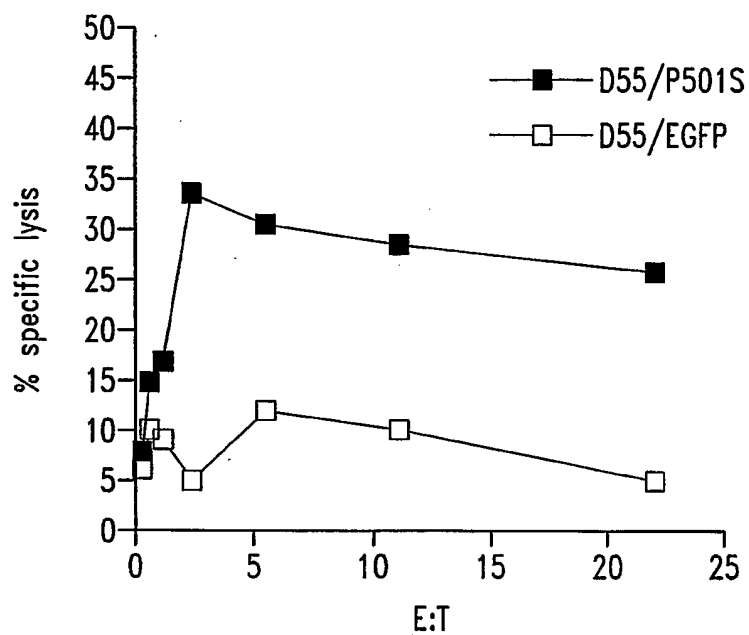
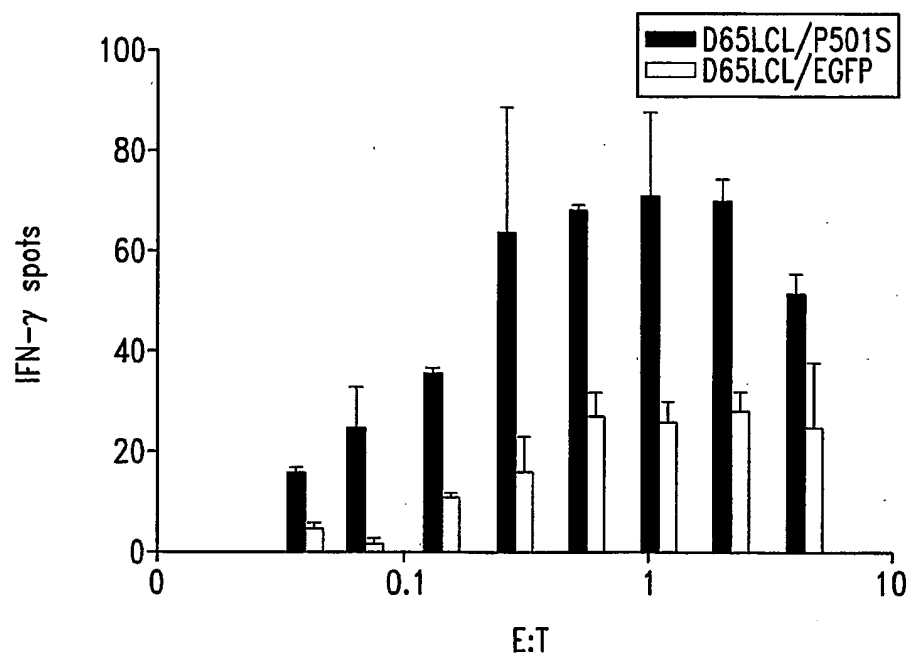


Fig. 3

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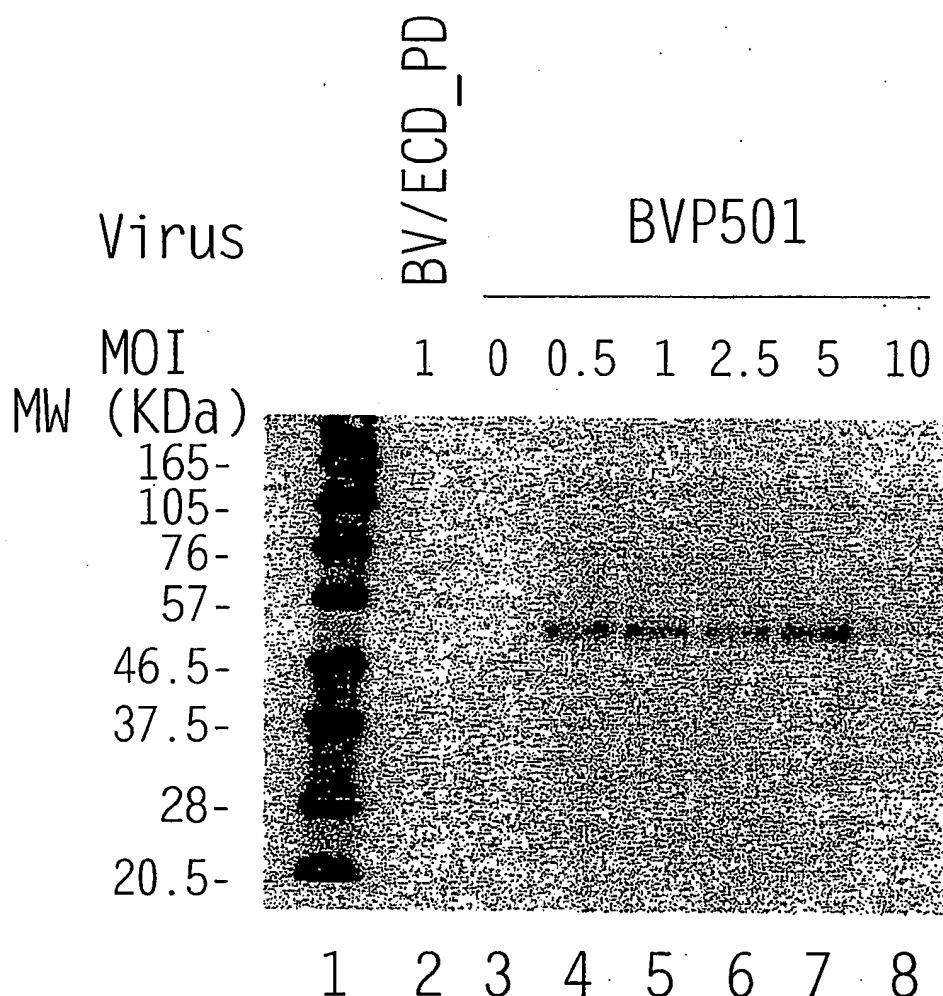
*Fig. 4**Fig. 5*

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*Fig. 6A**Fig. 6B*

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Expression of P501S
by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD_PD (lane2), without virus (lane3), or with recombinant baculovirus for P501 at different MOIs (lane 4-8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

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FIGURE 8. Mapping of the epitope recognized by 10E3-G4-D3

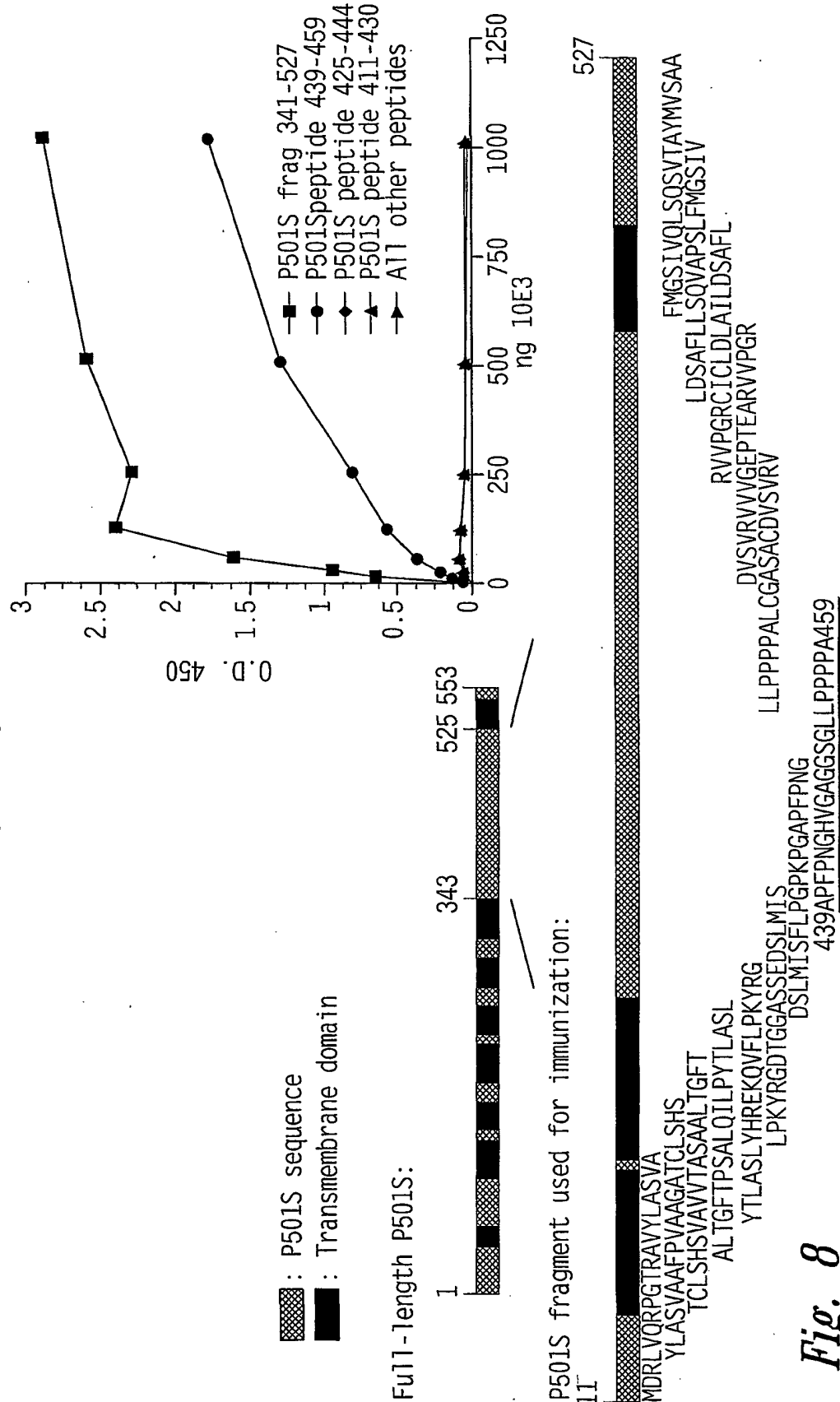


Fig. 8

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Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

MVQRLWVSRLLRHRK AQLLLVNLLTFGLEVCLAAGIT **YVPPLLLEVGVEEKFM**
TMVLGIGPVLGLVCYPLLGSAS

DHWRGRYGRRRP FIWALSLGILLSLFLIPRAGWL AGLLCPDPRPLE LALLILGVGLLDFCGQVCFTPL

EALLSDLFRDPDHCRQ AYSVYAFMISLGGCLGYLLPAI **DWDTSALAPYLGTQEE**

CLFGLLTILFLTCVAATLLV AEEAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL

HQLCCRMPTLR LFVAELCSWMALMTFTLFYTD VGEGLYQGVPRAEPTARRHYDEGVR

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VTAYMVSAAGLGLVAIYFAT *QVVF* **DKSDLAKYSA**

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:
Predicted extracellular domain; *Italic sequence*: Predicted intracellular
domain. Sequence in bold/underlined: used generate polyclonal rabbit
serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon
(1998) Principles Governing Amino Acid Composition of Integral Membrane
Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

Fig. 9

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Genomic Map of (5) Corixa Candidate Genes

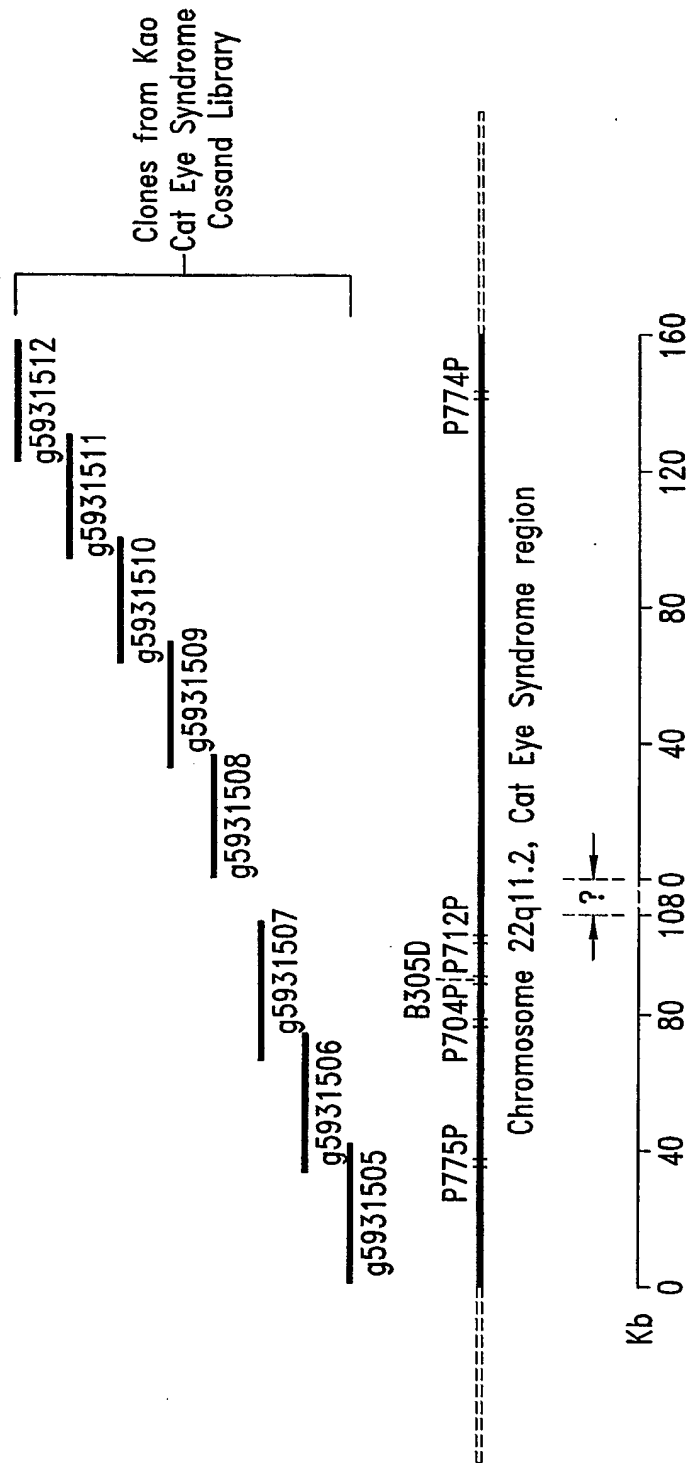
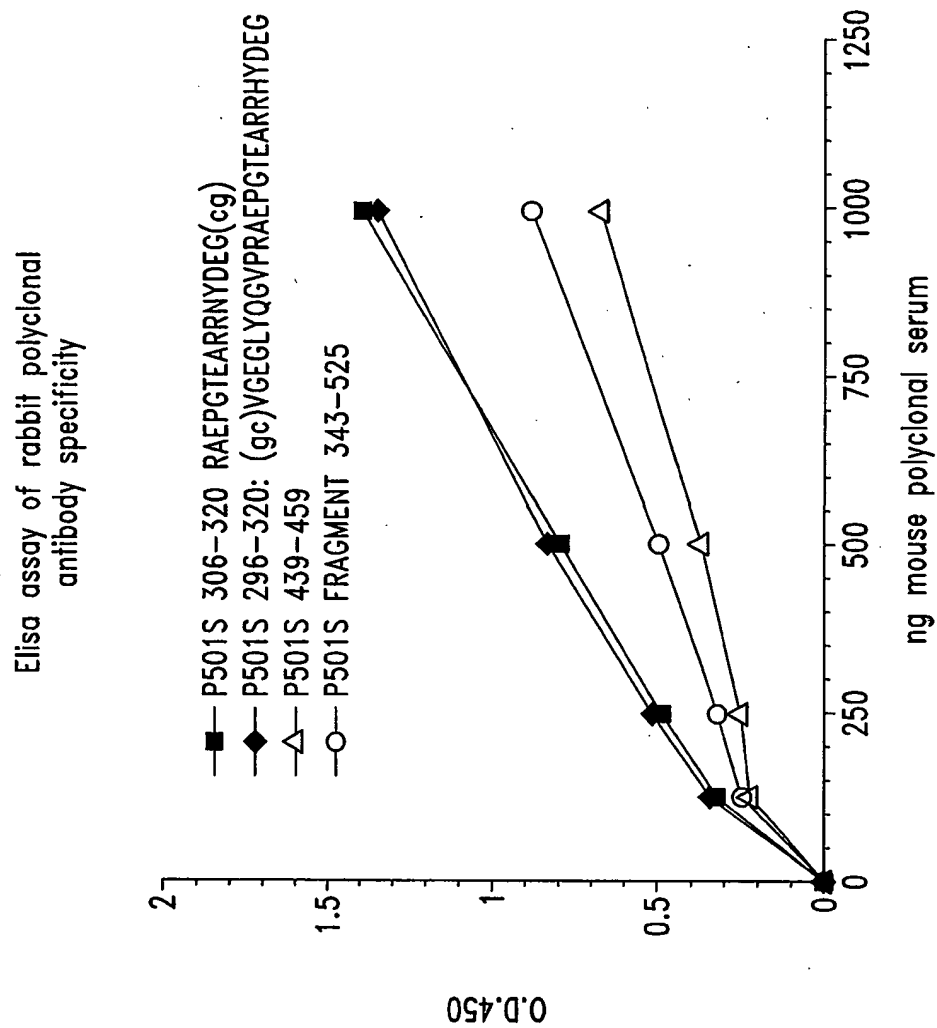


Fig. 10

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*Fig. 11*

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Fig. 12A (1)

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Fig. 12A (2)

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Fig. 12A (3)

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Fig. 12B

SEQUENCE LISTING

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 Xu, Jiangchun
 Dillon, Davin C.
 Mitcham, Jennifer L.
 Harlocker, Susan L.
 Yuqui, Jiang
 Kalos, Michael D.
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 Retter, Marc W.
 Stolk, John A.
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<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G

```

```

<400> 7
tttttttttt tttttttttt tggctctaga gggggtagag ggggtgctat agggtaaata      60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt      120
ggtttgctcc acagatttca gagcattgac cgtagtatac ccccggtcgt gtagcgggtga      180
aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaata gtggggacag      240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga      300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg      360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc      420
attggtggcc aattgatttg atggttaagg gagggatcgt tgaactcgtc tgttatgtaa      480
aggatncctt ngggatggga aggcnatnaa ggactangga tnaatggcgg gcangattatt      540
tcaaacngtc tctanttoct gaaacgtctg aaatgttaat aanaattaan tttngttatt      600
gaatnttng gaaaagggct tacaggacta gaaaccaaata angaaaanta atnntaangg      660
cnttatcntn aaaggtnata accnctccta tnatccacc caatngnatt cccacncnn      720
acnattggat nccccanttc canaaanggc cccccccgg tgnannccnc cttttgttcc      780
cttnantgan ggttattcnc cctngcntt atcancc      817

```

```

<210> 8
<211> 799
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

```

```

<400> 8
catttccggg tttactttct aaggaaagcc gagcggaagc tgctaacgtg ggaatcgggt      60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt      120
ctgaagcgca cgtcccagaa ggtggacttg gcaactgaaac agctgggaca catccgagag      180
tacgaacagc gcctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtcctgggg      240
tgggtggccg angcctganc cgctctgcct tgctgcccc angtgggccg ccacccctg      300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac cccacangg      360

```

ggattttgct	cctanantaa	ggctcatctg	ggcctcggcc	ccccacctg	gttggccttg	420
tctttgagnt	gagcccatg	tccatctggg	ccactgtcng	gaccaccttt	ngggagtgtt	480
ctccttacaa	ccacannatg	cccggctcct	cccggaaccc	antccancc	tgngaaggat	540
caagnccctgn	atccactnnt	notanaaccg	gccnccnccg	cngtggaacc	cnccttntgt	600
tccttttcnt	tnagggttaa	tnnccgcttg	gccttncan	ngtccnccn	ntttccnnt	660
gttnaaattg	ttangcnccc	nccnntcccn	cnncnncnan	cccgaccnnc	anntnnann	720
ncctgggggt	nccnncngat	tgaccenncc	nccctntant	tgcnttnggg	nncnntgccc	780
ctttccctct	nggganncg					799

<210> 9
 <211> 801
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(801)
 <223> n = A,T,C or G

<400> 9						
acgccttgat	cctccaggc	tgggactggt	tctgggagga	gccgggcatg	ctgtggtttg	60
taangatgac	actcccaaag	gtggctcctga	cagtggccca	gatggacatg	gggctcacct	120
caaggacaag	gccaccaggt	gcggggggccg	aagcccatat	gatccttact	ctatgagcaa	180
aatcccctgt	gggggcttct	ccttgaagtc	cgccancagg	gctcagtctt	tggaaccang	240
cagggtcatgg	ggttgtnngc	caactggggg	ccncaacgca	aaanggcnc	gggcctcngn	300
cacccatccc	angacgggc	tacactnctg	gacctccnc	tccaccactt	tcatgcgctg	360
ttontaccgc	cgnatntgtc	ccancgtgtt	cngtgccnac	tccanccttct	nggacgtgcg	420
ctacatacgc	ccggantcnc	nctcccgctt	tgtccctatc	cacgtncan	caacaaattt	480
cncctantg	caccnattcc	caenttttnc	agntttccnc	nncngcttc	cttntaaaag	540
ggttganccc	cggaaaatnc	cccaaagggg	ggggggcngg	tacccaactn	ccccctnata	600
gctgaantcc	ccatnaccnn	gnctcnatgg	ancntccnt	tttaannacn	ttctnaactt	660
gggaananc	ctcgnccntn	cccccnttaa	tccnccttg	cnangnncnt	cccccnntcc	720
ncccnntng	gentntnann	cnaaaaaggc	ccnnnancaa	tctcctnnnc	cctcanttgc	780
ccanccctcg	aatcggccn	c				801

<210> 10
 <211> 789
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(789)
 <223> n = A,T,C or G

<400> 10						
cagtctatnt	ggccagtgtg	gcagctttcc	ctgtggctgc	cggtgccaca	tgccgtgtccc	60
acagtgtggc	cgtggtgaca	gcttcagccg	ccctcaccgg	gttcaccttc	tcagccctgc	120
agatccctgc	ctacacactg	gcctccctct	accaccggga	gaagcagggt	ttcctgccca	180
aataccgagg	ggacactgga	ggtgctagca	gtgaggacag	cctgatgacc	agcttcctgc	240
caggccctaa	gcctggagct	cccttcccta	atggacacgt	gggtgctgga	ggcagtggcc	300
tgctcccacc	tccaccgcg	ctctgcgggg	cctctgcctg	tgatgtctcc	gtacgtgtgg	360
tggtgggtga	gccaccgan	gccaggggtg	ttccggggccg	gggcatctgc	ctggacctcg	420
ccatccctga	tagtgcttcc	tgctgtccca	ngtggcccca	tccctgttta	tggtgtccat	480
tgtccagctc	agccagtctg	tcaactgccta	tatggtgtct	gccgcaggcc	tggtgtgtgt	540
cccatttact	ttgctacaca	ggtantattt	gacaagaacg	anttggccaa	atactacgcg	600
ttaaaaaatt	ccagcaacat	tgggggtgga	aggcctgcct	cactgggtcc	aactccccgc	660
tcctgttaac	cccatggggc	tgccggcttg	gccgccaat	tctgttgctg	ccaaantnat	720

gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtnG 780
 ggngttccc 789

<210> 11
 <211> 772
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(772)
 <223> n = A,T,C or G

<400> 11
 cccaccctac ccaaataatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60
 tttgttaaata aaataagtta aatattttaa tgctgtgtc tctgtgatgg caacagaagg 120
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180
 tgtgggctga ggggacctg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata 240
 actttcatat gttcaaatacc catggaggag tgtttcatcc tagaaactcc catgcaagag 300
 ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt 360
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420
 ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc 480
 ctccctgtat aagtccagac tgaaccccc ttggaaggnc tccagtcagg cagccctana 540
 aactggggaa aaaagaaaag gacgccccan ccccagctg tgcanctacg cacctcaaca 600
 gcacaggggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720
 gggccnccac ccnaatntt gctgggaaat ttttctccc cttaattntt tc 772

<210> 12
 <211> 751
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 12
 gcccgaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa 60
 agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggg gcaggtttca 120
 ttggctgtgt tgggtgacgtt gtcatcgcaa cagaatgggg gaaaggcact gttctctttg 180
 aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240
 atggtgggtg tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
 ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac 360
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420
 acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna 480
 cncggctgc gatgaagaaa tnacccnccg ttgacaaact tgcattggc tggganccac 540
 agtggcccn aaaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgccactg 600
 ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct 660
 tnatnaacnt gaacctgcn tngtggctcc tggtcaggnc cnnngcctga cttctnaann 720
 aangaactcn gaagncccca cngganann g 751

<210> 13
 <211> 729
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(729)
 <223> n = A,T,C or G

<400> 13
 gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgcctt 60
 tgtggancct cagcagtncc ctctttcaga actcantgcc aagancctg aacaggagcc 120
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gtcacatctt 180
 ctgtgtggtg cagccctggt ggccagtggc atctgggtgt caatcgatgg ggcatccttt 240
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300
 ctcatgcag ccggcggtgt ggtcttagct ctaggtttcc tgggctgcta tgggtgctaag 360
 actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct 420
 gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt 480
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaaanact tcaactcaagt 540
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt 600
 gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa 660
 acgtcccccac cacagccaat tgaaaacctg caccacaacc aaanggttcc ccaaccanaa 720
 attnaaggg 729

<210> 14
 <211> 816
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(816)
 <223> n = A,T,C or G

<400> 14
 tgctcttctt caaagttggt cttgttgcca taacaaccac cataggtaaa gcgggcgag 60
 tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgagag tcctgtgtct 120
 ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtaaaag 180
 ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt ggggggtgtct 240
 tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga 300
 cangtgccag agcacactgg atggcgcctt tccatgnnan gggccctgng ggaaagtccc 360
 tganccccc anctgcctct caaangcccc accttgacac ccccgacagg ctagaatgga 420
 atcttcttcc cgaaaggtag ttnttcttgt tgcccancnc anccccntaa acaaactctt 480
 gcanatctgc tccngggggg tcntantacc ancggtggaa aagaacccca ggngcgaac 540
 caancctgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna 600
 ctgtnnanc ttagnccttg gtccctntgg gttgnncttg aacctaaten cennntcaact 660
 gggacaagg aantngccnt ccttttaatt cccnancntn ccccttggtt tgggggttttn 720
 cncnctccta cccagaaan nccgtgttcc cccccaacta ggggcnaaa cennntnttc 780
 cacaaccctn cccacccac gggttcngnt gggtng 816

<210> 15
 <211> 783
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(783)
 <223> n = A,T,C or G

<400> 15
 ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaaccctg gtgctgaagg 60

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atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga 120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga 180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca 240
ccaagcagac agaagactac tgccctcgcat ccaacaangt gggtcgctgc cggggctctt 300
tcccacgctg gtactatgac cccacggagc agatctgcaa gagtttcgtt tatggaggct 360
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctance tgtcnggggtg 420
tgcaagggtg gcctttgana ngcanctctg gggctcangc gactttcccc cagggccctt 480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gccacccag ttccgctgca 540
ncaatggctg ctgcacnac antttcctng aattgtgaca acacccccca ntgccccaa 600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccg 660
cncctcctt ttccccnntn aacaaagggc nctngcctt gaactgccn aaccnngaa 720
tctnccnng aaaaantncc cccctgggt cctnnaance cctcncnaa anctncccc 780
ccc 783

```

```

<210> 16
<211> 801
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

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```

<400> 16
gccccaatc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa 60
agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggg gcaggtttca 120
ttggctgtgt tgggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
aagtaggggt agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240
atgggtgtgt tccacacttg agtgaagtct tccgtgggaa cataatcttt cttgatggca 300
ggcactacca gcaacgtcag gaagtgtcga gccattgtgg tgtacaccaa ggcgaccaca 360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480
cngctgcga atgaaagaaa ntaccacagt tgacaaactg catggccact ggacgacagt 540
tgcccgaaan atcttcagaa aagggatgcc ccatcgattg aacaccana tgcccactgc 600
cnacaggggt gcncncnncn gaaagaatga gccattgaag aaggatcctc ntggctctaa 660
tgaactgaaa cntgcatgg tggccctgt tccagggtct tggcagtga ttctganaaa 720
aaggaacngc nttagcccc ccaaangana aaacaccccc ggggtgttgc ctgaattggc 780
ggccaaggan cctgccccn g 801

```

```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca gggtccctc tgccctgcca ctgagtggca acaccggga gctgttttgt 60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgttcca gtttcattaa gaccatgatg atcctcttca atttgctcat 180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgcctat cagtttgtca acgtgggcta 300
cttctcatc gcagccggcg ttgtgtgtct tgctcttggg ttccgtgggt gctatgggtg 360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcatctcat 420

```

tgctgaagtt	gcagctgctg	tggtgcgctt	ggtgtacacc	acaatggctg	aaccattcct	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	ttcccaggaa	aaattcactc	540
aantntggaa	caccnccatg	aaaagggctc	caatttctgn	tggttcccc	aactataccg	600
gaattttgaa	agantcnccc	tacttccaaa	aaaaaanant	tgcttttnc	ccnttctgt	660
tgcaatgaaa	acntoccaa	acngccaatn	aaaacctgcc	cnnncaaaaa	ggntcncaaa	720
caaaaaaant	nnaagggttn					740

<210> 18
 <211> 802
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(802)
 <223> n = A,T,C or G

<400> 18						
ccgctgggtt	cgctgggtcca	gngnagccac	gaagcacgtc	agcatacaca	gcctcaatca	60
caaggtcttc	cagctgccc	acattacgca	gggcaagagc	ctccagcaac	actgcatatg	120
ggatacactt	tacttttagca	gccagggtga	caactgagag	gtgtcgaagc	ttattcttct	180
gagcctctgt	tagtggagga	agattccggg	cttcagctaa	gtagtcagcg	tatgtcccat	240
aagcaaacac	tgtgagcagc	cggaaagtag	aggcaaagtc	actctcagcc	agctctctaa	300
cattgggcat	gtccagcagt	tctccaaaca	cgtagacacc	agnngccctc	agcacctgat	360
ggatgagtgt	ggccagcgct	gcccccttgg	ccgacttggc	taggagcaga	aattgctcct	420
ggttctgccc	tgtcaccttc	acttcgcac	tcactactgc	actgagtgtg	ggggacttgg	480
gctcaggatg	tccagagacg	tggttcgcgc	ccctcnctta	atgacaccgn	ccanncaacc	540
gtcggctccc	gccgantgng	ttcgctgtn	ctgggtcagg	gtctgctggc	cnctacttgc	600
aancctcgct	nggcccatgg	aattcaccnc	accggaactn	gtangatcca	ctnnttctat	660
aaccggncgc	caccgcnnnt	ggaactccac	tcttnttnc	ttacttgag	ggttaagggtc	720
acccttncg	ttacottggt	ccaaacctn	cctgtgtgc	anatngtnaa	tcnggncena	780
tnccanccnc	atangaagcc	ng				802

<210> 19
 <211> 731
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(731)
 <223> n = A,T,C or G

<400> 19						
cnaagcttcc	aggtnacggg	ccgnaancc	tgaccnagg	tancanaang	cagnncggg	60
gagcccaccg	tcacngngng	ngtctttat	nggagggggc	ggagccacat	cnctggacnt	120
cntgacccca	actcccnc	ncncantgca	gtgatgagt	cagaactgaa	ggtnacgtgg	180
caggaaccga	gancaaannc	tgctccnntc	caagtccgcn	nagggggcg	ggctggccac	240
gcncatccnt	cnagtgtgn	aaagcccenn	cctgtctact	tgtttgaga	acngcnnnga	300
catgcccagn	gttanataac	nggcngagag	tnantttgcc	tctcccttcc	ggctgcgcan	360
cgngtntgct	tagnggacat	aacctgacta	cttaactgaa	ccnngaatac	tnccnccct	420
ccactaagct	cagaacaaaa	aacttcgaca	ccactcantt	gtcacctgnc	tgctcaagta	480
aagtgtaccc	catncccaat	gtntgctnga	ngctctgncc	tgcnttangt	tcggctcctg	540
gaagacctat	caattnaagc	tatgtttctg	actgcctctt	gctccctgna	acaancnacc	600
cnnccntcca	agggggggnc	ggcccccaat	ccccccaacc	ntnaattnan	ttanccccc	660
ccccnggcc	cggcctttta	cnancntcnn	nnacngggna	aaaccnnngc	tttncccaac	720
nnaatccncc	t					731

10

<210> 20
 <211> 754
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(754)
 <223> n = A,T,C or G

<400> 20
 tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
 caacccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120
 annttaaatt aaatnttntt tggnggnnna anccnaatgt nangaaagtt naaccanta 180
 tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
 aaatngttna nggaaaaccc aantttctnt aaggttggtt gaaggntnaa tnaaaanccc 300
 nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360
 gggnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg 420
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntccggg 480
 ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat cctccnaga aaaaaanctc 540
 ccaggntgag nntnggggtt ncccccccc canggccct ctcgnanagt tggggtttgg 600
 ggggcctggg attttntttc cctnttnc tcccccccc ccngganag aggttngngt 660
 tttgntcnc ggcccnccn aaganccttn ccganttann ttaaaccnt gcctnggcga 720
 agtcnttgn agggntaaan ggccccctnn cggg 754

<210> 21
 <211> 755
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(755)
 <223> n = A,T,C or G

<400> 21
 atcancccat gaccccnac nngggaccnc tcancgggnc nnncnaccnc cggccnatca 60
 nngtnagnnc actncnnttn natcacnccc cncnactac gcccnananc cnacgcncta 120
 nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180
 ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240
 nncnncanat gattttcctn anccgattac ccntncccc tanccctcc cccccaacna 300
 cgaaggcnct ggnccnaagg nngcgncccc ccgctagntc cccncaagt cncncccta 360
 aactcancn nattacnccg ttcntgagta tcaactcccc aatctcacc tactcaactc 420
 aaaaanatcn gatacaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
 ttagnngtcc ntnaancntc ctaatacttc cagtctncct tcnccaattt cnaangget 540
 ctttcngaca gcatntttt gttcccnntt gggttcttan ngaattgcc ttctnngaac 600
 gggctcntct tttccttcgg ttancctggg ttcnccggc cagtattat ttccntttt 660
 aaattcntnc cntttanttt tggcnttca aacccccggc cttgaaaacg gccccctggt 720
 aaaaggttgt tttganaaaa tttttgttt gtcc 755

<210> 22
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 22

tttttttttt	tttttangtg	tngtcgtgca	ggtagaggct	tactacaant	gtgaanacgt	60
acgctnggan	taangcgacc	cganttctag	gannncacct	aaaatcanac	tgtgaagatn	120
atcctgnnna	cggaanggtc	accggnngat	nntgctaggg	tgneenctcc	cannncnttn	180
cataactcng	nggccctgcc	caccaccttc	ggcgggccng	ngnccgggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	ccccnncng	accnnggcga	tccgggggtnc	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccggnccc	ctttaccctt	nnacaagcca	360
cngcctctta	ncnccngccc	cccctccant	nngggggact	gccnanngt	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgctcgant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	gcccctaccc	ttcgtctcgg	nncacccttc	ccgacnanga	nccgtctccg	540
cncnccngng	cctcncctcg	caacaccgcg	ntctctcngt	ncggnnnccc	ccccaccgc	600
ncctctcncc	ngnccgnancn	ctccnccncc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggngacnng	nagcncnttc	gcncgcgcgn	gcgnccctt	cgcncngaa	720
ctnctctcng	ccantnncgc	tcaancnna	cnaaacgcg	ctgcgcggcc	cgnagcgncc	780
ncctccncca	gtcctcccg	cttccnacc	angnnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

gcgcaaaacta	tacttcgctc	gnactcgtgc	gcctcgtcnc	tcttttcttc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatchan	aagntcganc	agtccaaact	gantaacaca	120
cacacnncan	aganaaatcc	nctgccttcc	anagtanacn	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgccgcc	atntgtcnc	gtttattntn	ccagctcnc	240
ctnccnacc	tactctctcn	nagctgtcnn	accctngtn	cgnaccccc	naggtcgga	300
tcgggtttnn	nntgaccgng	cnccccctcc	ccccctccat	nacganccnc	ccgcaccacc	360
nanngcncgc	cccccgnnct	cttcgcnc	ctgtcctntn	ccccctgtngc	ctggcncngn	420
accgcattga	ccctcgccnn	ctncnngaaa	ncgnanacgt	ccgggttggn	annancgtg	480
tgggnnngcg	tctgcncgc	gttccttccn	ncncttcca	ccatcttct	tacnggtct	540
ccnccgcctc	tcnnncaenc	cctgggacgc	tnctcctntgc	cccccttnac	ccccccctt	600
cgncgtgncc	cgnccccacc	ntcatttnca	nacgntcttc	acaannncct	ggntnctcc	660
cnancngnncn	gtcanccnag	ggaaggngg	ggnnccnntg	nttgacgttg	ngngangtc	720
cgaanantcc	tcnccntcan	cntaccct	cgggcgnnct	ctcngttnc	aacttancaa	780
ntctcccccg	ngngcncntc	tcagcctcnc	ccccccnct	ctctgcantg	tnctctgctc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcattgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggtcnta	60
-------------	------------	------------	------------	------------	------------	----


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ccctgttgga attncgggga naccaaggga nccccctcct ccanctgtga aggaaaaann 540
gatggaattt tnccttccg gccnntcccc tcttccttta cagccccct nntactctc 600
tccctctntt ntccgtncnc acttttnacc cennnatttc ccttnattga tcggannctn 660
ganattccac tnnccgctnc cntcnatcng naanacnaaa nactntctna cccnggggat 720
gggnnccctcg ntcatectct ctttttctct accnccnntt ctttgectct ccttngatca 780
tccaacctc gntggccntn ccccccnntt tcttttncce 820

```

```

<210> 27
<211> 818
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(818)
<223> n = A,T,C or G

```

```

<400> 27
tctgggtgat ggcctcttcc tcctcaggga cctctgactg ctctgggcca aagaatctct 60
tgtttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120
ctgcgggatgc tgtgacggac ccaaggggca aatagggtcc caggggtccag ggaggggagc 180
ctgctgagca cttccgcccc tcaccctgcc cagccctgc catgagctct gggctgggtc 240
tcgcctcca gggttctgct cttccangca ngccancaag tggcgtggg ccacactggc 300
ttcttctctg cccntccctg gctctganc tctgtcttcc tgtcctgtgc angcnccttg 360
gatctcagtt tccctcnctc anngaactct gttctgann tcttcantta actntgantt 420
tatnacnna tggnctgtnc tgcnnactt taatgggcn gaccggctaa tccctccctc 480
nctcccttcc anttcnnna accngcttnc cntctctcc cntancccg ccngggaanc 540
ctcctttgcc ctnaccang gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc 600
ctgntnnccc cncctcncnt tncctcgtcc cncnncgc nngcannttc ncngtcccn 660
tnnctctttn ngntcgnaa ngntcnctn tnnnnngnc ngntnntn tccctctcnc 720
cnnntgnang tnnntnnnc ncngncccc nnnnnnnnn nggnntnnn tctnncngc 780
ccnncccc ngnattaagg cctccnntct ccggccnc 818

```

```

<210> 28
<211> 731
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 28
aggaaggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg 60
tcccaacatg anggtgnngt tctcttttga angagggttg ngtttttann ccnggtgggt 120
gattnaaccc cattgtatgg agnnaaagg ttttagggat ttttcggctc ttatcagtat 180
ntanattcct gtnaatcgga aaatnatntt tcnnncggaa aatnttgctc ccatccgnaa 240
atttctccg ggtagtgc atntnggggn cngccangtt tcccaggctg ctanaatcgt 300
actaaagntt naagtggan tncaaatgaa aacctnnac agagnatccn taccgactg 360
tnnnttncct tcgccctntg actctgcnn agcccaatac ccnngnngat gtcnccnng 420
nnngcgcnc tgaaannnc tcgnggctnn gancatcang gggtttcgca tcaaaagcnn 480
cgtttcncat naaggcact tngcctcat caaccnctng cctcnmcca tttngccgtc 540
nggttcncct acgctnntng cncctnnntn ganattttnc ccgcctngg naancctcct 600
gnaatgggta gggncctntc ttttnaccnn gnggtntact aatcnctnc acgcntnctt 660
tctnaccccc ccccttttt caatcccanc ggcnaatggg gtctcccnng cgangggggg 720
nnnccann c 731

```

14

<210> 29
 <211> 822
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(822)
 <223> n = A,T,C or G

<400> 29
 actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat 60
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt 120
 atntntacnc tcatanncct cmnacccac tccctcttaa cccntactgt gcctatngcn 180
 tnnctantct ntgcgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc 240
 tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn 300
 tccatnantt annntaacta ccaactgacnt ngactttcnc atnanctcct aatttgaatc 360
 tactctgact cccacngcct annnattagc ancntccccc nacnatntct caaccaaadc 420
 ntcaacaacc tatctantctg ttcnccaacc nttncctccg atccccnnac aacccccctc 480
 ccaaataccc nccacctgac nccaaaccn caccatcccg gcaagccnan ggcatttan 540
 ccaactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600
 aatnctcctn naatttactn ncantnccat caanccacn tgaaacnaa cccctgtttt 660
 tanatccctt ctttcgaaaa ccnaccctt annncccaac ctttngggcc ccccnctnc 720
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780
 canatcctat cccttanttn ggggnccctt nccngggcc cc 822

<210> 30
 <211> 787
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(787)
 <223> n = A,T,C or G

<400> 30
 cgggcgctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120
 gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna 180
 gctggaagcc ctggagggcc tctctcgcca gcctccccct tctctccag ctctccangg 240
 acaccagggg ctocaggcag cccattattc ccagnangac atgggtgttc tccacgcgga 300
 cccatggggc ctgnaaggcc agggctcctt ttgacaccat ctctcccgtc ctgcctggca 360
 ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt 420
 tccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tntttcctgt 480
 gtgaaattgt ttntccctc ncnatccnc ncnacatacn aaccgggaan cataaagtgt 540
 taaagcctgg gggtnccctn nngaanaac tnaactcaat taattgcgtt ggctcatggc 600
 ccgctttccn ttcnngaaaa ctgtentccc ctgcnttntt gaatcgcca ccccccnggg 660
 aaaagcggtt tgcnttttng ggggntcctt ccncttccc cctcnctaan cctnccgct 720
 cggtcgttnc nggtngcggg gaangggnat nnnctccnc naaggggng agnnngntat 780
 ccccaaa 787

<210> 31
 <211> 799
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(799)
 <223> n = A,T,C or G

<400> 31
 tttttttttt ttttttttgc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac 60
 catgtaccag ggctattaga agcaagaagg aaggaggagg ggcagagcgc cctgctgagc 120
 aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct 180
 cccgcagggt gggggccacc agtccagggt tgggagcact acanggggtg ggagtgggtg 240
 gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca 300
 ggggaccttc tgttctccca nggnaacttc nttnatctcn aaagaacaca actgtttctt 360
 cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca 420
 tatggttccg gcccacctct cccntcnaaa aagtaattca ccccccccn cctctnttg 480
 cctgggccct taantaccca caccggaact canttannta ttcatcttng gntgggcttg 540
 nttnatcnccn cctgaangcg ccaagttgaa aggccacgcc gtncnctc cccatagnan 600
 nttttnnnt canctaagtc cccccnggc aacnatcaa tcccccccn tgggggcccc 660
 agccanggc ccccgntcgc ggnnnccngn cncgnantcc ccaggntctc ccantcngnc 720
 ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnnncac 780
 ctgcccccc cccnccgng 799

<210> 32
 <211> 789
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(789)
 <223> n = A,T,C or G

<400> 32
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 ttttncnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac 120
 ggcaacaggc tccggcgcg gcggcgcgcc cctacctgc ggtaccaa atngcagcctc 180
 cgctcccgt tgatnttct ctgcagctgc aggatgcctt aaaaacaggc ctcgcccntn 240
 ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc 300
 nattaggaat agtggtnnta cccnccnccg ttggcncact cccntggaa accacttntc 360
 gcggctccg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt 420
 nccngccaca atcatnactc agactggcnc gggtgtggcc caaaaaancn ccccaaaacc 480
 ggnccatgtc ttncgggggt tgctgcnatn tncatcacct cccgggcnc ncaggncac 540
 ccaaaagttc ttngggcccn caaaaaancn cccgggggnc ccagtttcaa caaagtcac 600
 ccccttggcc cccaaatcct cccccgntt nctgggttg ggaacccacg cctctnnctt 660
 tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnctctaa ngaaaacncc 720
 ntctnnnca ccatcccccc nngnnacgnc tancaangna tccctttttt tanaaacggg 780
 cccccncc 789

<210> 33
 <211> 793
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(793)
 <223> n = A,T,C or G

<400> 33
 gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg 60

```

aattcatggc tgttggagca atanaacccc agttctacga gctgctgac aaaggacttg 120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana 180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg 240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca 300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac 360
ctctgctggt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggcgtaatc atggtcatan ctgtttctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaattt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncctccc gctttctcgc ttctgaant ccttcccccc ggtctttcgg cttgcccna 780
acggtatcna cct 793

```

```

<210> 34
<211> 756
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(756)
<223> n = A,T,C or G

```

```

<400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtga accgtaaaag cccaatctt 60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgta catactggag 180
atcggggccc aatggagcat cctacgcaan gacatccct ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttctg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtgcc tgcccanga catacanacc aatgtctaca tcnaccacca 420
gtgtcctgga gcaatactga tgganggcag ctaccncaa gtnttcttg ccnagggtaa 480
catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg 600
atnctnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttncct 660
ttactgaggg ttnattgccg cccttgccgt tatcatggtc acnccngttn cctgtgttga 720
aattnttaac cccccacaat tccacgcna cattng 756

```

```

<210> 35
<211> 834
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(834)
<223> n = A,T,C or G

```

```

<400> 35
gggatctct anactnacct gnatgcatgg ttgtcgggtg ggtcgtgtc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggt gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cnetcttggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct cggtagaactc gatgacnang ggcagctggg tgtgtntgat 240
aaantccanc angttctcct tggtagacctc cccttcaaag ttgttccggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactggt 360
ggaaactgat cccaaatggg atgtcatcca tcgctctgc tgcctgcaa aaacttgctt 420
ggcncaaata cgactcccn tccttgaaag aagccnatca caccctcct cctggactcc 480

```

17

```

nncaangact ctnccgctnc cccntccnng caggggttggt ggcannccgg gcccntgcgc 540
ttcttcagcc agttcactnat ntctcatcagc ccctctgccca gctgttntat tccttggggg 600
ggaanccgctc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcncnt 660
acntnctggg ccgggttcaa antccctccn ttgncnntcn cctcgggcca ttctggattt 720
nccnaacttt ttccctcccc cnccccnccg ngtttggnntt ttccatnggg ccccaactct 780
gctnttggcc antcccttgg gggcntntan cnccccctnt ggtcccntng ggcc 834

```

```

<210> 36
<211> 814
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(814)
<223> n = A,T,C or G

```

```

<400> 36
cggncgcttt cngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacn 60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca 120
naagcccaac tcaggccatt cctaccaaag gaagaaaggc tgggtctctcc acccctgta 180
ggaaaggcct gccttgtaag acaccacaat nccgctgaat ctnaagtctt gtgttttact 240
aatggaaaaa aaaaataaac aanagggtttt gttctcatgg ctgccaccg cagcctggca 300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca 360
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480
aggggagtc ntttncagtg gatctgccaa anantaccn tatcatcnnt gaataaaaag 540
gcccctgaac ganatgcttc cancanctt taagaccat aatcctngaa ccatgggtgc 600
cttccggtct gatccnaag gaatgttctt ggggtccant cctcctttg ttnccttacgt 660
tgtnttgac cnttgctngn atnaccaan tganatcccc ngaagcacc tnccttggc 720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnaa 780
ngngaactca agaaggtctn ngaaaaacca cncn 814

```

```

<210> 37
<211> 760
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(760)
<223> n = A,T,C or G

```

```

<400> 37
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60
gcgcagtgtt cgctgaagg gttgtagtac cagcgcgga tgctctcctt gcagagtctt 120
gtgtctggca ggtccacgca atgcccttg tctactggga aatggatgcg ctggagctcg 180
tcnaanccac tcgtgtattt ttacangca gcctctccg aagcntccg gcagttgggg 240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat 360
cncctnancc caaactgcct ctcaaaggcc accttgaca ccccgacagg ctagaaatgc 420
actcttctc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aaccaaaanc 480
ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt ggggaaanaa acccgcngn 540
gancncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca 600
caattgaact gttaacnttg ggccngttc cncnnggtg gtctgaaact aatcaccgtc 660
actgaaaaa ggtangtgc ttccctgaat tcccaaant cccctngntt tgggtnttt 720
ctcctctncc ctaaaaatcg tnttcccccc cntanggcg 760

```


18

<210> 38
 <211> 724
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(724)
 <223> n = A,T,C or G

<400> 38
 tttttttttt tttttttttt tttttttttt ttttttaaaaa cccctcccat tgaatgaaaa 60
 cttccnaaat tgtccaaccc cctcncccaa atnccattt cggggggggg gttccaaacc 120
 caaattaatt ttgganttta aattaaatnt tnattnnggg aanaanccaa atgtnaagaa 180
 aatttaaccc attatnaact taaatnccn gaaacccntg gnttccaaaa atttttaacc 240
 cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggtt 300
 ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt 360
 tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt 420
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tcccnttttg gggccatncc 480
 ccncttttcg gggtttggn ntaggttgaa tttttnnang ncccaaaaaa nccccaana 540
 aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttg gaaaggnggg 600
 tttntggggg ccngggantt cnttccccn ttncncccc cccccnggt aaanggttat 660
 ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccggnncg 720
 gccg 724

<210> 39
 <211> 751
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 39
 tttttttttt tttttctttg ctcacattta atttttatnt tgattttttt taatgctgca 60
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120
 tttatttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180
 ggccgcctta agctttctaa atttgaaca tctaagcaag ctgaanggaa aaggggggtt 240
 cgcaaaatca ctgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300
 ttaactgctt gtacaattac ntctacttt taattaattg tgctnaangc ttttaattana 360
 cttgggggtt ccctcccan accaaccnccn ctgacaaaaa gtgccngccc tcaaatnatg 420
 tcccggcnnt cnttgaacaa cacngcngaa ngttctcatt ntccccncnc caggtnaaaa 480
 tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn 540
 ccctcaancn aattnctnng ccccggtcnc gentnngtcc cncccgggct cggggaantn 600
 cacccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660
 cnnagactnt cctcnncnan cncaattttc ttttntcac gaacncgnnc cnnaaaatgn 720
 nnnncnctc cncnngtcn naatcnccan c 751

<210> 40
 <211> 753
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(753)

<223> n = A,T,C or G

<400> 40

gtggtatttt	ctgtaagatc	agggtgttcct	ccctcgtagg	tttagaggaa	acaccctcat	60
agatgaaaac	cccccgaga	cagcagcact	gcaactgcc	agcagccggg	gtaggagggg	120
cgccctatgc	acagctgggc	ccttgagaca	gcagggcttc	gatgtcaggc	tcgatgtcaa	180
tgggtctggaa	gcgccggctg	tacctgcgta	ggggcacacc	gtcagggccc	accaggaact	240
tctcaaagtt	ccaggcaacn	tcgttgcgac	acaccggaga	ccaggtgatn	agcttggggg	300
cggtcataa	cgcggtggcg	tcgtcgctgg	gagctggcag	ggcctcccgc	aggaaggcna	360
ataaaagggtg	cgccccgcga	ccgttcanc	cgcacttctc	naanaccatg	angttgggct	420
cnaaccacc	accannccgg	acttccttga	nggaattccc	aaatctcttc	gntcttgggc	480
ttctnctgat	gccctanctg	gttgcccngn	atgccaanca	nccccaancc	ccgggggtcct	540
aaanaccn	cctctctntt	tcctctgggt	tnttntcccc	ggacctgggt	tcctctcaag	600
ggancccata	ttctnaccan	tactcaccnt	nccccccnt	gnnaccanc	cttctanngn	660
ttcccncccg	ncctctggcc	cntcaaan	gcttnacna	cctgggtctg	ccttcccccc	720
tnccctatct	gnaccn	tttgtctcan	tnt			753

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

actatatcca	tcacaacaga	catgcttcat	cccatagact	tcttgacata	gcttcaaagt	60
agtgaaccca	tccttgattt	atatacatat	atgttctcag	tattttggga	gcctttccac	120
ttctttaaac	cttggtcatt	atgaacactg	aaaataggaa	tttgtgaaga	gttaaaaagt	180
tatagcttgt	ttacgtagta	agtttttgaa	gtctacattc	aatccagaca	cttagttgag	240
tgttaaactg	tgatttttaa	aaaatatcat	ttgagaatat	tctttcagag	gtattttcat	300
ttttactttt	tgatttaattg	tgttttatat	attagggtag	t		341

<210> 42

<211> 101

<212> DNA

<213> Homo sapien

<400> 42

acttactgaa	tttagttctg	tgctcttcct	tatttagtgt	tgtatcataa	atactttgat	60
gtttcaaaca	ttctaaataa	ataattttca	gtggcttcat	a		101

<210> 43

<211> 305

<212> DNA

<213> Homo sapien

<400> 43

acatctttgt	tacagtctaa	gatgtgttct	taaatcacca	ttccttctg	gtcctcaccc	60
tcagggtgg	tctcacactg	taattagagc	tattgaggag	tctttacagc	aaattaagat	120
tcagatgcct	tgctaagtct	agagttctag	agttatgttt	cagaaagtct	aagaaaccca	180
cctcttgaga	ggtcagtaaa	gaggacttaa	tatttcatat	ctacaaaatg	accacaggat	240
tggtacaga	acgagagtta	tcctggataa	ctcagagctg	agtacctgcc	cgggggccgc	300
tcgaa						305

<210> 44

<211> 852

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(852)
 <223> n = A,T,C or G

<400> 44
 acataaatat cagagaaaag tagtctttga aatattttacg tccaggagtt ctttgtttct 60
 gattattttg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt 120
 ctctccatcc tggggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct 180
 ccagaatttc tctttttag tagtatctca tagctcggct gagcttttca taggtcatgc 240
 tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300
 agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct gggttcaaga 360
 ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc 420
 acttggcagg ggggtcttgc tcttttttca tatcagggtga ctctgcaaca ggaagggtgac 480
 tgggtgttgc catggagatc tgagcccgcc agaaagtttt gctgtccaac aaatctactg 540
 tgctaccata gttgggtgtca tataaatagt tctngtcttt ccagggtgttc atgatggaag 600
 gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tccactactgc 660
 actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg 720
 ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctcgccgttg atgtcgaact 780
 cntggaaaag gatacaattg gcatccagct ggttgggtgc caggaggtga tggagccact 840
 cccacacctg gt 852

<210> 45
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 45
 acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60
 agtctgacac catccggagc atcagcattg cttcgcagtg cctaccgcg gggaactctt 120
 gcctcgtttc tggctggggg ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg 180
 tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgaccgc ctgt 234

<210> 46
 <211> 590
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(590)
 <223> n = A,T,C or G

<400> 46
 actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta 60
 atttgatagc aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa 120
 aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180
 tgantataac taattgacaa tggaaaatca attttaattg gaattgcaca ttatccttta 240
 aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat 300
 caggataaan aactgaaggg canaaagaat taattttcac ttcagttaac ncaccanatt 360
 ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc 420
 tggctcttaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480
 ggctcctgtt atatcccaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540
 gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt 590

<210> 47
 <211> 774
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(774)
 <223> n = A,T,C or G

<400> 47
 acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60
 tgaacagaat tttcctgnac aacgggggctt caaaataatt ttcttgggga ggttcaagac 120
 gcttcaactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180
 cattacagac gggactcttg gaggaaggat aaacagaaag gggacaaaag ctaatcccaa 240
 aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggtctt 300
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtcccagg ctctgtgtgtg 360
 ctgggtcctg gtcttcagcc cccagctctg gaagcccacc ctctgtgat cctgcgtggc 420
 ccacactcct tgaacacaca tcccaggtt atattccttg acatggctga acctcctatt 480
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540
 acggcatggg aagcctttct gacttgcctg attactccag catcttgaa caatccctga 600
 ttccccactc cttagaggca agataggggtg gtttaagagta gggctggacc acttgagcc 660
 aggctgctg cttcaaattn tggtcattt acgagctatg ggaccttggg caagtnatct 720
 tcacttctat gggontcatt ttgttctacc tgcaaatgg gggataataa tagt 774

<210> 48
 <211> 124
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(124)
 <223> n = A,T,C or G

<400> 48
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120
 tggt 124

<210> 49
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 49
 gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60
 tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120
 ttagggcacc catatcccaa gcantgt 147

<210> 50
 <211> 107
 <212> DNA
 <213> Homo sapien

<400> 50
 acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatatgtc 60

atggtttgag gttaggagga gttaggcata tgttttggga gaggggt 107

<210> 51
 <211> 204
 <212> DNA
 <213> Homo sapien

<400> 51
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgacagg 60
 cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgcca 180
 cctccctttt gggaccagca atgt 204

<210> 52
 <211> 491
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(491)
 <223> n = A,T,C or G

<400> 52
 acaaagataa catttatctt ataacaaaaa tttgatatgtt ttaaagggtta gtattgtgta 60
 gggatattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120
 ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180
 aaaaacttctt gtatcaattt cttttgttca aaatgactga ctttaantatt tttaaatatt 240
 tcanaaacac ttctcaaaa attttcaana tggtagcttt canatgtnc ctcagtccca 300
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360
 atgcaacagt gtcttttctt tnccttttct ttttttttt ttacaggcac agaaactcat 420
 caattttatt tggataacaa aggtctcca aattatattg aaaaataaat ccaagttaat 480
 atcactcttg t 491

<210> 53
 <211> 484
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(484)
 <223> n = A,T,C or G

<400> 53
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60
 gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac 120
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180
 caatcaaact tctacataac actatagtaa ttaaaacggt aaaaaaaagt gttgaaatct 240
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300
 agctttgant tttttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct 360
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg 420
 tancctgant ctgtgtattc caggancagg cggtatggaat gggccagccc ncggtgttc 480
 cant 484

<210> 54
 <211> 151
 <212> DNA

<213> Homo sapien

<400> 54

actaaacctc	gtgcttgga	actccataca	gaaaacgggtg	ccatccctga	acacggctgg	60
ccactgggta	tactgctgac	aaccgcaaca	acaaaaacac	aaatccttgg	cactgggctag	120
tctatgtcct	ctcaagtgcc	tttttgtttg	t			151

<210> 55

<211> 91

<212> DNA

<213> Homo sapien

<400> 55

acctggcttg	tctccgggtg	gttccggcg	ccccccacgg	tccccagaac	ggacactttc	60
gccctccagt	ggatactcga	gccaaagtgg	t			91

<210> 56

<211> 133

<212> DNA

<213> Homo sapien

<400> 56

ggcggatgtg	cgttggttat	atacaaatat	gtcattttat	gtaagggact	tgagtatact	60
tggatttttg	gtatctgtgg	gttgggggga	cggccagga	accaataccc	catggatacc	120
aagggacaac	tgt					133

<210> 57

<211> 147

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(147)

<223> n = A,T,C or G

<400> 57

actctggaga	acctgagccg	ctgctccgcc	tctgggatga	ggtgatgcan	gcngtgggcg	60
gactgggagc	tgagcccttc	cctttgcgcc	tgccctcagag	gattgttgcc	gacntgcana	120
tctcantggg	ctggatncat	gcagggt				147

<210> 58

<211> 198

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(198)

<223> n = A,T,C or G

<400> 58

acagggatat	aggtttinaag	ttattgtnat	tgtaaaatac	attgaatfff	ctgtatactc	60
tgattacata	cattttatcct	ttaaaaaaga	tgtaaatcct	aatttttatg	ccatctatta	120
atttaccat	gagttacctt	gtaaatgaga	agtcataata	gcactgaatt	ttactagtt	180
ttgacttcta	agtttggt					198

<210> 59

24

<211> 330
 <212> DNA
 <213> Homo sapien

<400> 59
 acaacaaatg ggttgtagg aagtcttata agcaaaactg gtgatggcta ctgaaaagat 60
 ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt 120
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180
 tacagtcaat aaatgacaaa gccaggcct acaggtgggt tccagacttt ccagaccag 240
 cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt 300
 tttcgtcttt attggacttc tttgaagagt 330

<210> 60
 <211> 175
 <212> DNA
 <213> Homo sapien

<400> 60
 accgtgggtg ccttctacat tctgaaggc tcttcacca acatctggtt ctacttcggc 60
 gtcgtgggct ccttctctt catcctcatc cagctgggtc tgctcatcga ctttgcgac 120
 tcttgaacc agcggtaggt gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61
 <211> 154
 <212> DNA
 <213> Homo sapien

<400> 61
 accccacttt tctcctgtg agcagtctgg acttctcact gctacatgat gagggtagt 60
 ggttggtgct cttcaacagt atcctccctt ttccggatct gctgagccgg acagcagtgc 120
 tggactgcac agccccgggg ctccacattg ctgt 154

<210> 62
 <211> 30
 <212> DNA
 <213> Homo sapien

<400> 62
 cgctcgagcc ctatagtgag tcgtattaga 30

<210> 63
 <211> 89
 <212> DNA
 <213> Homo sapien

<400> 63
 acaagtcatt tcagcacctt ttgctcttca aaactgacca tcttttatat ttaatgcttc 60
 ctgtatgaat aaaaatgggt atgtcaagt 89

<210> 64
 <211> 97
 <212> DNA
 <213> Homo sapien

<400> 64
 accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60
 aatcagtgc tccaggattg gtccttgat ctggggt 97

<210> 65
 <211> 377
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(377)
 <223> n = A,T,C or G

<400> 65
 acaacaanaa ntcccttctt taggcactg atggaaacct ggaacccct tttgatggca 60
 gcatggcgctc ctaggccttg acacagcggc tgggggtttg gctntccaa accgcacacc 120
 ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcaggg 180
 tcggtcataa natgaaatcc caanggggac agaggctcagt agaggaagct caatgagaaa 240
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccg 300
 tgggggtgaa ctaccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360
 gggcgggagg agcatgt 377

<210> 66
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 66
 acgcctttcc ctccagaattc agggaagaga ctgtgcctg ccttctctcg ttgttgctg 60
 agaaccctg tgccccttc caccatatcc accctcgctc catctttgaa ctcaaacacg 120
 aggaactaac tgcaccctgg tctctctccc agtccccagt tcaccctcca tccctcacct 180
 tctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggtt 240
 ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300
 tggtt 305

<210> 67
 <211> 385
 <212> DNA
 <213> Homo sapien

<400> 67
 actacacaca ctccacttgc ctttgtgaga cactttgtcc cagcacttta ggaatgctga 60
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120
 cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180
 tgtgtctgtc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcaactctcag atgcccatac 360
 catagtttct gtgctagtgg accgt 385

<210> 68
 <211> 73
 <212> DNA
 <213> Homo sapien

<400> 68
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaa tgaaaataaa 60
 gtttttttaa tgg 73

<210> 69
 <211> 536
 <212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttggggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgtctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
ccgggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtccct	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccccta	acagggggccc	totcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcacttccac	tcataaacgc	tcctcatact	aggcctaacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggg	cttcgatacg	ggataatcct	atttattacc	tcagaagttt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtgtt	aaaaagaaaa	tctccagcaa	gcattctcatt	240
taaaataaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gaccctaacta	ataattatta	gaaatacatt	taaaaacatc	gagtacatca	360
agtcagtgtt	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacac	agtatataag	gctgtaaaaa	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(511)
 <223> n = A,T,C or G

<400> 72
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta 60
 aaatgaaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180
 aaacatggan agattggtgc tgganacgc cgtggctatt cctcattgtt attacanagt 240
 gaggttctct gtgtgccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420
 atttctctcc attgcagcna naaaccggtt cttctaagca aacncagggtg atgatggcna 480
 aaatacacc cctcttgaag naccnggagg a 511

<210> 73
 <211> 499
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(499)
 <223> n = A,T,C or G

<400> 73
 cagtgccagc actggtgcc a gtaccagtag caataacagt gccagtgcc gtgccagcac 60
 cagtgggtggc ttcagtgtg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120
 tggccttggg ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180
 caagttagat tttagatatt gttaatcctg ccagtctttc tcttcaagcc aggggtgcac 240
 ctcagaaacc tactcaacac agcactctag gcagccaact tcaatcaatt gaagttgaca 300
 ctctgcattt aatctatttg ccatttctga aaaaaaaaaa aaaaaaagg cggccgctcg 360
 antctagagg gcccgtttaa acccgctgat cagcctogac tgtgccttct anttgccagc 420
 catctgttgt ttgcccctcc cccgntgcct tccttgacct tggaaagtgc cactcccact 480
 gtcccttctc aantaatat 499

<210> 74
 <211> 537
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(537)
 <223> n = A,T,C or G

<400> 74
 tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat 60
 ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact 120
 tocaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180
 cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga 240
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300
 ggctttttag ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc 360
 cagtttgcct gatataattg ttgatattaa gattcttgac ttatattttg aatgggttct 420
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480
 tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgt 537

<210> 75
 <211> 467
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(467)
 <223> n = A,T,C or G

<400> 75
 caaanacaat tgttcaaaaag atgcaaataa tacactactg ctgcagctca caaacacctc 60
 tgcattattac acgtacctcc tcctgctcct caagtagtgt ggtctatatt gccatcatca 120
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
 tggcacaagg aggccatctt ttctcatcgt gttattgtcc ctagaagcgt cttctgagga 240
 tctagttggg ctttctttct gggtttgggc catttcantt ctcattgtgt tactattcta 300
 tcattattgt ataacggtt tcaaaccngt gggcacncag agaaccctac tctgtaataa 360
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420
 ctocagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76
 <211> 400
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(400)
 <223> n = A,T,C or G

<400> 76
 aagctgacag cattcggggc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60
 tctctcttc tggcctggag gctatccagc gtactccaaa gattcaggtt tactcacgct 120
 atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag 240
 acttgtcttt cagcaaggac tggctcttct atctcttgta ctacactgaa ttcaccccca 300
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77
 <211> 248
 <212> DNA
 <213> Homo sapien

<400> 77
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
 ccagctgccc cggcggggga tgcgaggtc ggagcaccct tgcccggctg tgattgtctc 120
 caggcactgt tcatctcagc ttttctgtcc ctttgtccgc ggcaagcgt tctgctgaaa 180
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgtctcac ccgaaaaaaa 240
 aaaaaaaa 248

<210> 78
 <211> 201
 <212> DNA
 <213> Homo sapien

<400> 78

29

```

actagtccag tgtgggtggaa ttccattgtg ttggggcccaa cacaatggct acctttaaca      60
tcacccagac cccgccctgc cgtgcccaca cgctgctgct aacgacagta tgatgcttac      120
tctgtactac ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct      180
gatttaaaaa aaaaaaaaaa a                                     201

```

```

<210> 79
<211> 552
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(552)
<223> n = A,T,C or G

```

```

<400> 79
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg      60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt      120
cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag      180
tgtgatagta taagtatcta agtgcagatg aaagtgtggt atatatatcc attcaaaatt      240
atgcaagtta gtaattactc aggtttaact aaattacttt aatatgctgt tgaacctact      300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga      360
taatattcta tgtttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta      420
ttcccaggaa tatgggggttc atttatgaat antaccggg anagaagttt tgantnaaac      480
cngtttttgt taatacgtta atatgtcctn aatnaacaag gcntgactta tttocaaaaa      540
aaaaaaaaaa aa                                             552

```

```

<210> 80
<211> 476
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 80
acaggggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga      60
ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct      120
cacacagact ccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt      180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta      240
agggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac      300
tcttctaagt cctcttccag cctcactttg agtcctcctt gggggttgat aggaantntc      360
tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat      420
gctgaaaaaa ttaaaatggt ctgggttcnc tttaaaaaaa aaaaaaaaaa aaaaaa      476

```

```

<210> 81
<211> 232
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

```

```

<400> 81

```

```

tttttttttg tatgcntcn ctgtgnggtt attgttgctg ccacctgga ggagcccagt    60
ttcttctgta tctttctttt ctgggggata ttcttggtc tgcccctcca ttcccagcct    120
ctcatcccca tcttgcaact ttgttagggg tggaggcgct ttcttggtag cccctcagag    180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct          232

```

```

<210> 82
<211> 383
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

```

```

<400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc    60
agtaccagta ccaataacat gccagtgccg gtgccagcac cagtgtgtggc ttcaagtctg    120
gtgccagcct gaccgcact ctcacatttg ggctcttcgc tggccttggt ggagctggtg    180
ccagcaccag tggcagctct ggtgcctgtg gttctctcta caagtgagat tttagatatt    240
gttaatcctg ccagtcctttc tcttcaagcc aggggtgcata ctcagaaacc tactcaacac    300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg    360
ccatttcaaa aaaaaaaaaa aaa          383

```

```

<210> 83
<211> 494
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

```

```

<400> 83
accgaatttg gaccgctggc ttataagcga tcatgtcttc cagtattacc tcaacgagca    60
gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc    120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa    180
acgcttcaag gtgctcatga cccagcaacc gcgccctgtc ctctgagggg ccttaactg    240
atgtcttttc tgccacctgt taccctctcg agactccgta accaaactct tcggactgtg    300
agccctgatg cctttttgccc agccatactc tttggcntcc agtctctcgt ggcgattgat    360
tatgcttggt tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt    420
tttncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactotta    480
aaaaaaaaa aaaa          494

```

```

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca    60
agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag    120

```

```

gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgcaa ctggctgggtg 240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgcctggcac ttgctcattg 300
ccatgttcag ttacacattc ggcaaagtag agggcaacag cnatctctac tgggaaggcc 360
agcgtnnccg cctcatccgg 380

```

```

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

```

```

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
tnccatcgct atactgtagg tttgccacca cctcctgcat ctggggcgcg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagttag gtcaccagcc 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
ccagattctg cattaccaga nagcogtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcctggaagt gctngccgct cctcgctcct tgggtggnngc gcntnccttt 480
t 481

```

```

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
acttggaana gcaacttnaa gcctggacac tgggtattaaa attcacaata tgcaacactt 120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taaggggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtccg aaaaaagcaa aagtaaagag ttnttaattt gttagccaat tcactttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cttttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

```

```

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

```

<400> 87

```

```

agaaccagtg atctctnaaa acaacctctc ataccttggt gacctaatgt tgtgtgcgtg      60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg      120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaaggtg actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg      300
ggggacaaaag aaaagcanaa ctgaacatna gaaacaattn cctgggtgaga aattncataa      360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt              413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcggtt cctctctatc tagctccagc ctctcgcttg cccactccc cgcgctccgc      60
gtcctagccn accatggcgg ggcccctgcg cgcccctgtg ctctgtgtgg ccacccctggc      120
cgtggccctg gccgtgagcc ccgcgccggg ctccagtcgc ggcaagccgc cgcgctggt      180
gggaggccca tggacccgcg gtggaagaag aaggtgtgct gcgtgcactg gactttgccg      240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc      300
cccaancaaa ttgttactng gggtaanata ttcttggaag ttgaacctgg gccaaacnng      360
ttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg      420
gaancantcc tgnctctttc caaat      448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattggggc aggatgcttt gagtttatca      60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc      120
agaggtctag gtctgcatat cagcagacag ttgttccgtg tattttgtag ccttgaagtt      180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcac      240
tttnatgtn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg      300
ttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn      360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn      420
aattcnana anttcagntn tcatacaaca naacngganc ccc              463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

```

```

<400> 90
agggattgaa ggtctntnt actgtcggac tgttcancca ccaactctac aagttgctgt      60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat      120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact      180
tccttttgta agacttcac tcgttaaagtc ttaagttttg tagaaaggaa ttaattgct      240
cgttctctaa caatgtcctc tccttgaagt atttggtga acaaccacc tnaagtccct      300
ttgtgcatcc attttaata tacttaatag ggcattggtg cactagggtta aattctgcaa      360
gagtcactctg tctgcaaaag ttgcgttagt atatctgcc      400

```

```

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

```

```

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcctcttt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nnccgctctt      180
tgtggaaaaa ctggcacttg notggaacta gcaagacatc acttacaat tcacccacga      240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt      300
tgtcaatact aaccgctgg tttgcctcca tcacatttgt gatctgtagc tctggataca      360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt      420
ngatcagggt cccatttccc agtcogaatg ttcacatggc atatnttact tcccacaaaa      480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

```

```

<400> 92
atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact      60
ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt      120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg gggtgacggt      180
taantgcagg aagaggctga ccacctcgcg gtocaccagg atgcccgact gtgcgggacc      240
tgcagcga aa ctcctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca      300
gaaccttccg cctgttctct ggcgctcacct gcagctgctg ccgctnacac tcggcctcgg      360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgctcc      420
aggaacggcn ccagcgtgtc caggtcaatg tcgggtgaanc ctccgcgggt aatggcg      477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

```



```

<400> 93
gaacggctgg accttgccgc gcattgtgct gctggcagga ataccttggc aagcagctcc      60
agtcgagca gccccagacc gctgccgccc gaagctaagc ctgcctctgg ccttccccctc      120
cgctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn      180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa      240
caacaacaaa ataacatggt tgcctgttna gttgtataaa agtangtgat tctgtatnta      300
aagaaaatat tactgttaca tatactgctt gcaanttctg tattttattgg tncctctggaa      360
ataaatatat tattaaa                                     377

```

```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg ggttagggtc cagttcccag tggagaagaa aggccaggag aantgctgctc      60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgaccctc      120
ccaaggaaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg      180
gaaggcccca ttccggggct gttcccgcag gaggaaggga aggggctctg tgtgcccccc      240
acgaggaana ggccctgant cctgggatca nacaccocct cactgtatc cccacacaaa      300
tgcaagctca ccaaggtccc ctctcagtc cttccctaca ccctgaacgg nactggccc      360
acaccacccc agancancca cccgccatgg ggaatgtncct caaggaaatcg cngggcaacg      420
tggaactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana      480
aaaaaaaaana aaaaaa                                     495

```

```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 95
ggttacttgg ttccattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt      120
tagctgtttt gatttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact      180
tattttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt      240
atgatgaaaa gcaatagata tatattcttt tattatgtnn aattatgatt gccattatta      300
atcggaacaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac      360
ttgggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata      420
tttanttcan taatttcttt cttgtttac gtttaattttg aaaagaatgc at              472

```

```

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

```

35

<222> (1)...(476)

<223> n = A,T,C or G

<400> 96

ctgaagcatt	tcttcaaact	tntctacttt	tgtcattgat	acctgtagta	agttgacaat	60
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<210> 97

<211> 479

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(479)

<223> n = A,T,C or G

<400> 97

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<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

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<211> 171

<212> DNA

<213> Homo sapien

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<210> 108
 <211> 382
 <212> PRT
 <213> Homo sapien

<400> 108

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35      40      45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50      55      60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65      70      75      80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85      90      95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
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Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115     120     125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130     135     140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145     150     155     160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165     170     175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180     185     190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195     200     205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg

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Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala		
	260	265
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Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val		
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His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu		
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Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala		
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Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu		
	340	345
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<210> 109

<211> 1524

<212> DNA

<213> Homo sapien

<400> 109

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<211> 3410

<212> DNA

<213> Homo sapien

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ctccctctta	ctctctctag	gactgggctg	atgaaggcac	tgcccaaaat	ttcccttacc	3000
cccaactttc	ccctaccccc	aactttcccc	accagctcca	caacctgtt	tggagctact	3060
gcaggaccag	aagcacaaaag	tgcggtttcc	caagcctttg	tccatctcag	ccccagagt	3120
atatctgtgc	ttggggaatc	tcacacagaa	cactaggagc	acccctgcc	tgagctaaag	3180
gaggctttat	ctctcagggg	gggtttaagt	gccgttttga	ataatgtcgt	cttattttat	3240
tagcgggggtg	aatattttat	actgtaagtg	agcaatcaga	gtataatgtt	tatgggtgaca	3300

aaattaaagg ctttcttata tgttttaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3360
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaataa aaaaaaaaaa 3410

<210> 111
 <211> 1289
 <212> DNA
 <213> Homo sapien

<400> 111
 agccaggcgt ccctctgcct gcccaactcag tggcaacacc cgggagctgt tttgtccttt 60
 gtggagcctc agcagttccc tctttcagaa ctcaactgcc agagccctga acaggagcca 120
 ccattgcagt cttcagcttc attaaagacca tgatgatcct cttcaatttg ctcatctttc 180
 tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcaccccttc 240
 tgaagatctt cgggccactg tcgtccagtgc ccatgcagtt tgtcaacgtg ggctacttcc 300
 tcatcgcagc cggcgttgtg gtctttgtct ttgggttccct gggtgctat ggtgctaaga 360
 ctgagagcaa gtgtgccctc gtgacgttct tcttcacccct cctcctcatc ttcatgtctg 420
 aggttgacgc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttctgacgt 480
 tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt 540
 ggaacaccac catgaaaggc ctcaagtgcgt gtggcttcac caactatacg gattttgagg 600
 actcacccta cttcaaagag aacagtgcct ttccccatt ctgttgcaat gacaacgtca 660
 ccaacacagc caatgaaacc tgcaccaagc aaaaggetca cgaccaaaaa gtagagggtt 720
 gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag 780
 ctggaattgg gggcctcgag ctggctgccca tgattgtgtc catgtatctg tactgcaatc 840
 tacaataagt ccacttctgc ctctgccact actgctgccca catgggaact gtgaagaggc 900
 accctggcaa gcagcagtga ttgggggagg ggacaggatc taacaatgtc acttgggcca 960
 gaatggacct gccctttctg ctccagactt ggggctagat agggaccact ccttttagcg 1020
 atgcctgact ttccttccat tgggtgggtg atgggtgggg ggcattccag agcctctaag 1080
 gtagccagtt ctgttgccca ttccccagt ctattaaacc cttgatatgc cccctaggcc 1140
 tagtggtgat ccagtgctc tactggggga tgagagaaag gcattttata gcctgggcat 1200
 aagtgaaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc 1260
 tgttacaatg ttaaaaaaaa aaaaaaaaaa 1289

<210> 112
 <211> 315
 <212> PRT
 <213> Homo sapien

<400> 112
 Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
 1 5 10 15
 Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
 20 25 30
 Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
 35 40 45
 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
 50 55 60
 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
 65 70 75 80
 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
 85 90 95
 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
 100 105 110
 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
 115 120 125
 Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
 130 135 140
 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
 145 150 155 160

Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
 165 170 175
 Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Arg Gln
 180 185 190
 Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu
 195 200 205
 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
 210 215 220
 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
 225 230 235 240
 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
 245 250 255
 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
 260 265 270
 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
 275 280 285
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly
 290 295 300
 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
 305 310 315

<210> 113
 <211> 553
 <212> PRT
 <213> Homo sapien

<400> 113
 Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
 1 5 10 15
 Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu
 20 25 30
 Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val
 35 40 45
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
 50 55 60
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
 65 70 75 80
 Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
 85 90 95
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
 100 105 110
 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
 115 120 125
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
 130 135 140
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
 145 150 155 160
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
 165 170 175
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
 180 185 190
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
 195 200 205
 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
 210 215 220
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
 225 230 235 240
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu

43

245 250 255
 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg
 260 265 270
 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
 275 280 285
 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
 290 295 300
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
 305 310 315 320
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
 325 330 335
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
 340 345 350
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
 355 360 365
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 370 375 380
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
 385 390 395 400
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 545 550

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
 1 5 10 15
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20 25 30
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
 85 90 95

Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
 130 135 140
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
 145 150 155 160
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
 165 170 175
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
 180 185 190
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
 195 200 205
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
 210 215 220
 Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
 225 230 235 240
 Gln

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400> 115
 gctctttctc tcccctctc tgaatttaat tctttcaact tgcaatttgc aaggattaca 60
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180
 actggttagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggt 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300
 tctctacatg cataacaaac cctgctocaa tctgtcacat aaaagtctgt gacttgaagt 360
 ttagtc 366

<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G
 <400> 116
 acaaagatga accatttcct atattatagc aaaattaaaa tctacccgta ttctaattatt 60
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120
 agactttact attttcatat ttttaagacac atgatttatc ctatttttagt aacctgggtc 180
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>

45

<221> misc_feature
 <222> (1)...(305)
 <223> n = A,T,C or G

<400> 117
 acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca 60
 tatttatcct cctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120
 aataaggcaa aatatatgaa acaacaggtc togagatatt ggaaatcagt caatgaagga 180
 tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt 240
 gactgccccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat 300
 tgggt 305

<210> 118
 <211> 71
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(71)
 <223> n = A,T,C or G

<400> 118
 accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa 60
 aantctggg t 71

<210> 119
 <211> 212
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(212)
 <223> n = A,T,C or G

<400> 119
 actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca 60
 gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac 120
 agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant 180
 aatggantca aganactccc aggcctcagc gt 212

<210> 120
 <211> 90
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(90)
 <223> n = A,T,C or G

<400> 120
 actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttggc 60
 ctccgccggc gcagaacatg ctggggtggt 90

<210> 121
 <211> 218

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(218)
<223> n = A,T,C or G

<400> 121
tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga 60
gaataagatt tgctaaaaga tttggggcta aaacatgggtt attgggagac atttctgaag 120
atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc 180
agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122
<211> 171
<212> DNA
<213> Homo sapien

<400> 122
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg 60
catttgtag ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt 120
caccaccccg gcggggtcat ctgtgccaca ggtccctggt gacagtgcgg t 171

<210> 123
<211> 76
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(76)
<223> n = A,T,C or G

<400> 123
tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca 60
ttatcaanta ttgtgt 76

<210> 124
<211> 131
<212> DNA
<213> Homo sapien

<400> 124
acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg 120
ttaagatttg t 131

<210> 125
<211> 432
<212> DNA
<213> Homo sapien

<400> 125
actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg 60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact ttgtctcaga tgctgaagaa 120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240

```

ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300
catggtgggg gtcttgcacg tgtaagaatg gaattgattt tgcttttgca agaattctcag 360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420
ctctttgctt gt 432

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<210> 126
<211> 112
<212> DNA
<213> Homo sapien

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<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60
agtaagaatg atatttcccc ccagggatca ccaaataattt ataaaaattt gt 112

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<210> 127
<211> 54
<212> DNA
<213> Homo sapien

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<400> 127
accacgaaac cacaacaag atggaagcat caatccactt gccaagcaca gcag 54

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<210> 128
<211> 323
<212> DNA
<213> Homo sapien

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<400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
ttctctctga agtctaggtt acccattttg gggaccattt ataggcaata aacacagttc 180
ccaaagcatt tggacagttt cttgtttgtt tttagaatgg ttttcctttt tcttagcctt 240
ttcctgcaaa aggtctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
aggtctgcctt cttttccatg tcc 323

```

```

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(192)
<223> n = A,T,C or G

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```

<400> 129
acatacatgt gtgtatatatt ttaaatatca cttttgtatc actctgactt tttagcatatc 60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180
gataaacaaa gt 192

```

```

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature

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48

<222> (1)...(362)

<223> n = A,T,C or G

<400> 130

ccctttttta	tggaatgagt	agactgtatg	tttgaanatt	tanccacaac	ctctttgaca	60
tataatgacg	caacaaaaag	gtgctgttta	gtcctatggt	tcagtttatg	cccctgacaa	120
gtttocattg	tgttttgccc	atctttctgg	taatcgtggg	atcctccatg	ttattagtaa	180
ttctgtattc	cattttgtta	acgcctggta	gatgtaacct	gctangaggc	taactttata	240
cttattttaa	agctcttatt	ttgtggtcat	taaaatggca	atttatgtgc	agcactttat	300
tgcagcagga	agcacgtgtg	ggttggttgt	aaagctcttt	gctaattctta	aaaagtaatg	360
gg						362

<210> 131

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(332)

<223> n = A,T,C or G

<400> 131

ctttttgaaa	gatcgtgtcc	actcctgtgg	acatcttgtt	ttaatggagt	ttcccatgca	60
gtangactgg	tatggttgca	gctgtccaga	taaaaacatt	tgaagagctc	caaatgaga	120
gttctcccag	gttcgccctg	ctgctccaag	tctcagcagc	agcctctttt	aggaggcatc	180
ttctgaacta	gattaaggca	gcttgtaa	ctgatgtgat	ttggtttatt	atccaactaa	240
cttccatctg	ttatcactgg	agaaagccca	gactcccan	gacnggtacg	gattgtgggc	300
atanaaggat	tgggtgaagc	tggcgttgtg	gt			332

<210> 132

<211> 322

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(322)

<223> n = A,T,C or G

<400> 132

acttttgcca	ttttgtatat	ataaacaatc	ttgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggctaag	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaattcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggt	180
tttagcaagt	taaaatgaan	atgacaggaa	aggcttattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	agggaagcct	300
gtaacaatct	acaattggtc	ca				322

<210> 133

<211> 278

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 133
 acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt 60
 cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta 120
 ctatttataa aaaatcaca atctttccct ttaagctatg ttnaattcaa actattcctg 180
 ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt 240
 cccacgaaac actaataaaa accacagaga ccagcctg 278

<210> 134
 <211> 121
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(121)
 <223> n = A,T,C or G

<400> 134
 gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60
 tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg 120
 t 121

<210> 135
 <211> 350
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(350)
 <223> n = A,T,C or G

<400> 135
 acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60
 atancaagt gtgactgggt aagcgtgcga caaaggctcag ctggcacatt acttgtgtgc 120
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180
 ggggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgtc 240
 ccacctcaat caagccctgg gccatgctac ctgcaatttg ctgaacaaac gtttgctgag 300
 ttcccaagga tgcaaagcct ggtgctcaac tcttggggcg tcaactcagt 350

<210> 136
 <211> 399
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(399)
 <223> n = A,T,C or G

<400> 136
 tgtaccgtga agacgacaga agttgcatgg cagggacagc gcagggccga ggccagggtt 60
 gctgtgattg tatccgaata ntccctcgtg gaaaagataa tgagatgacg tgagcagcct 120
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180
 cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag 240
 aaaactgcag aggccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc 300
 tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

50

<210> 137
 <211> 165
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(165)
 <223> n = A,T,C or G

<400> 137
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120
 ttggctggtc ccactggtgg tcaactgtcat tggtaggggt cctgt 165

<210> 138
 <211> 338
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(338)
 <223> n = A,T,C or G

<400> 138
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccac 120
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180
 tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt 240
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139
 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 139
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga 120
 attcaaacag acctcgatcat tcttggtgtg agcctggctg gctcaccgcc tatcatctgc 180
 atttgcttca ctcaggtgct accggactct ggccctgat gtctgtagtt tcacaggatg 240
 ccttatttgt cttctacacc ccacagggcc cctacttct tcggatgtgt ttttaataat 300
 gtcagctatg tgcccatcc tccttcacgc cctccctccc tttcctacca ctgctgagtg 360
 gcctggaact tgtttaaagt gt 382

<210> 140
 <211> 200
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(200)
 <223> n = A,T,C or G

<400> 140
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60
 acttttcat taaacanttt tgtaaagtgt caggctgcac ttgctccat anaattattg 120
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180
 atattcagca taaaggagaa 200

<210> 141
 <211> 335
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (335)
 <223> n = A,T,C or G

<400> 141
 actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggttg 60
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc aggggtttgtt 120
 atgcatgtag agaaccctaa ctaattttatt aaacaggata gaaacaggct gtctgggtga 180
 aatgggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240
 tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaaa agcaagatgg 300
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142
 <211> 459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (459)
 <223> n = A,T,C or G

<400> 142
 accaggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60
 ggggtgtttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120
 ctgatggaga aaacactgag ttttgacaaa tottatttta ttcagatagc agtctgatca 180
 cacatggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc 240
 ttcaaacatc atagccaatg atgcccgcgt tgcctataat ctctccgaca taaaaccaca 300
 tcaacacctc agtggccacc aaaccattca gcacagcttc cttactgtg agctgtttga 360
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420
 cagcanggtt gggaggaacc agctcaacct tggcgtant 459

<210> 143
 <211> 140
 <212> DNA
 <213> Homo sapien

<400> 143
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccacca totccctgag 120
 accatccgac ttccctgtgt 140

<210> 144
 <211> 164
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(164)
 <223> n = A,T,C or G

<400> 144
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg 120
 aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt 164

<210> 145
 <211> 303
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 145
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60
 actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat 120
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgcctgtg tgattaccat 300
 caa 303

<210> 146
 <211> 327
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(327)
 <223> n = A,T,C or G

<400> 146
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60
 actggcctgg agtgactcat tgctctgggt ggttgagaga gtccttttgc caacaggcct 120
 ccaagtcagg gctgggattt gtttcccttc cacattctag caacaatatg ctggccactt 180
 cctgaacagg gaggggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc 240
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300
 taggggtgag ctgtgtgact ctatggt 327

<210> 147
 <211> 173
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(173)
 <223> n = A,T,C or G

<400> 147

```

acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg      60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt      120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt              173

```

<210> 148

<211> 477

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(477)

<223> n = A,T,C or G

<400> 148

```

acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct      60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact      120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg      180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac      240
nccanccac ctcaccgacc ccacccctct acacagctac ctcccttgctc tctaacccca      300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag      360
caccactggt aagccttctc cagccaacac acacacacac acacncacac acacacatat      420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttacctgct atggtgg          477

```

<210> 149

<211> 207

<212> DNA

<213> Homo sapien

<400> 149

```

acagttgtat tataatatca agaaataaac ttgcaatgag agcattttaag agggaagaac      60
taacgtatnt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct      120
gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca      180
tttcaggcag agggaacagc agtgaaa

```

<210> 150

<211> 111

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(111)

<223> n = A,T,C or G

<400> 150

```

accttgatnt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg      60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t              111

```

<210> 151

<211> 196

<212> DNA

<213> Homo sapien

<400> 151

```

agcgcggcag gtcatttga acattccaga tacctatcat tactcgatgc tgttgataac      60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat      120
ggataccaac cggaaaaccc ctatcccgca cagcccactg tgggtccccc tgtctacgag      180

```

gtgcatccgg ctcagt 196

<210> 152
<211> 132
<212> DNA
<213> Homo sapien

<400> 152
acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagAAC 60
cttccccttt tcatctagt gtggaaacct gatgctttat gttgacagga atagaaccag 120
gagggagttt gt 132

<210> 153
<211> 285
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(285)
<223> n = A,T,C or G

<400> 153
acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag 60
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120
gcacatcaat aaagtccaaa gtcttggaact tggccttggc ttggaggaag tcatcaacac 180
cctggctagt gaggggtgcg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca 240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt 285

<210> 154
<211> 333
<212> DNA
<213> Homo sapien

<400> 154
accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac 120
cctaagccgg ttacacagct aactccact ggccctgatt tgtgaaattg ctgctgcctg 180
attggcacag gagtgcgaag tgttcagctc ccctcctcgg tggaaagaga ctctgatttg 240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg 300
gtcaggcctg tctcatccat atggatcttc cgg 333

<210> 155
<211> 308
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(308)
<223> n = A,T,C or G

<400> 155
actggaaata ataaaaccca catcacagt tttgtgtcaaa gatcatcagg gcatggatgg 60
gaaagtgtct tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat 120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc 180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggct 240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcagtctg 300

gccctggt 308

<210> 156
 <211> 295
 <212> DNA
 <213> Homo sapien

<400> 156
 accttgctcg gtgcttgga catattagga actcaaaata tgagatgata acagtgccta 60
 ttattgatta ctgagagaac tgtagacat ttagttgaag attttctaca caggaaactga 120
 gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgccct cattctatgt 180
 ctaatatatt ctcaatcaaa taaggtttagc ataatcagga aatcgaccaa ataccaatat 240
 aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295

<210> 157
 <211> 126
 <212> DNA
 <213> Homo sapien

<400> 157
 acaagtttaa atagtgtgt cactgtgcat gtgtgaaat gtgaaatcca ccacatttct 60
 gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc 120
 cttagt 126

<210> 158
 <211> 442
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(442)
 <223> n = A,T,C or G

<400> 158
 acccactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg 60
 aanccagcag gctgcccta gtcagtcctt ccttcagag aaaaagagat ttgagaaagt 120
 gcctgggtaa ttcaccatta atttctccc ccaaactctc tgagtcttcc cttaatattt 180
 ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta 240
 natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg 300
 ccaaccctgt tttccagtc caogtagaca gattcacagt gcggaattct ggaagctgga 360
 nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg 420
 tgttcattct ctgatgtcct gt 442

<210> 159
 <211> 498
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(498)
 <223> n = A,T,C or G

<400> 159
 acttccaggt aacgttggtt tttccgttga gcctgaactg atgggtgacg ttgtaggttc 60
 tccaacaaga actgaggttg cagagcgggt aggggaagagt gctgttccag ttgcacctgg 120
 gctgctgtgg actgttggtt attcctcact acggcccaag gttgtggaac tggcanaaag 180

```

gtgtgttgtt gganttgagc tcgggcggtt gtggtaggtt gtgggctctt caacaggggc 240
tgctgtggtg ccgggangtg aangtggtgt gtcacttgag cttggccagc tctggaaagt 300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa 360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn 420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc 480
aagggaataa gctgtggt 498

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac 60
agcttcagga tacttcagg agacagagcc accagcagca aaacaaatat tcccatgcct 120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc 180
cactagacat ctcatcagcc acttgtgtga agagatgcc catgacccca gatgcctctc 240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg 300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa 360
ctttagaat gaagcctgga 380

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca 60
cactgtccac tggcccttta tccacttggt gcttaatccc tcgaaagagc atgt 114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtthta atatcctcat atatatcaaa 60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt 120
tggtgatata taacttggca ataaccagct ctggtgatac ataaaactac tcaactgt 177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

```

```

<400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac 60
canagaaggc agctaaggct actcctacat cctggcgtgg gtggccttgc cctgcacctt 120

```

catcagcggc atgatgt

137

<210> 164

<211> 469

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (469)

<223> n = A,T,C or G

<400> 164

ottatcacaa	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacctt	cgtgacttta	60
tgcaatgcat	catgctatct	cataccta	gagggagttc	caggagattc	aaccaggaaa	120
tgcatggatc	tcaaaggaaa	caaacaccca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	caaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgt	360
tctagttagc	acagggctcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacacttt		469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (195)

<223> n = A,T,C or G

<400> 165

acagtttttt	atanatatcg	acattgcccg	cacttgtgtt	cagtttcata	aagctgggtg	60
atccgctgtc	atccactatt	ccttggctag	agtaaaaatt	attcttatag	cccatgtccc	120
tgcaggccgc	ccgcccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (383)

<223> n = A,T,C or G

<400> 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggctcga	gtccacacca	ccggtgtagg	tgtgctcaat	cttgggcttg	gcgcccacct	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgacagacc	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcagggtg	240
gatgccaaacc	tcgtctangg	tcggtgggaa	gctgggtgtcc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

<210> 167

58

<211> 247
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(247)
 <223> n = A,T,C or G

<400> 167
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat 60
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120
 tatanccata cacagagcca actctcaggg caaggcnatg gttggggcag anccagagac 180
 tcaatctgan tccaaagtgg tggctggaac actggctcatg acanaggcag tgactctgac 240
 tgangtc 247

<210> 168
 <211> 273
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(273)
 <223> n = A,T,C or G

<400> 168
 acttctaagt ttcttagaag tggaaggatt gtantcatcc tgaaaatggg ttactttcaa 60
 aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120
 gctgacacct gagcctgnat ttactcatcc ccttgagaag ccctttccag taggggtggc 180
 aattcccaac ttcttgcca caagcttccc aggttttctc ccctggaaaa ctccagcttg 240
 agtcccagat acactcatgg gctgccctgg gca 273

<210> 169
 <211> 431
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(431)
 <223> n = A,T,C or G

<400> 169
 acagccttgg cttcccaaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acagggttcta 120
 ctactgtcaa atgacccccc atacttcctc aaaggctgtg gtaagttttg cacagggtgag 180
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccaactgac 240
 cttgccatgg gcaaaaggcc ctaccacaaa aacaatagga tcaactgctgg gcaccagctc 300
 acgcacatca ctgacaaccg ggatggaaaa agaantgcc aactttcatac atccaactgg 360
 aaagtgatct gatactggat tottaattac cttcaaaagc ttctgggggc catcagctgc 420
 tcgaacactg a 431

<210> 170
 <211> 266
 <212> DNA
 <213> Homo sapien

59

<220>
 <221> misc_feature
 <222> (1)...(266)
 <223> n = A,T,C or G

<400> 170
 acctgtgggc tgggctgtta tgccctgtgcc ggctgctgaa agggagttca gaggtggagc 60
 tcaaggagct ctgcaggcat tttgccaaanc ctctccanag canagggagc aacctacact 120
 ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat 180
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240
 tcaaagctag gggctctggca ggtgga 266

<210> 171
 <211> 1248
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1248)
 <223> n = A,T,C or G

<400> 171
 ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca 60
 ctggctcatgg aaaacgaatt gttctgctcg ggcgctcctgg tgcattccgca gtgggtgctg 120
 tcagccgcac actgtttcca gaagtgtgtg cagagctcct acaccatcgg gctgggcctg 180
 cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta 240
 cggcaccag agtacaacag acccttgctc gctaaccgacc tcatgctcat caagttggac 300
 gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360
 gcgggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420
 gtgctgcagt gcgtgaacgt gtcggtgggtg tctgaggagg tctgcagtaa gctctatgac 480
 ccgctgtacc accccagcat gttctgcgcc ggcgaggggc aagaccagaa ggactcctgc 540
 aacggtgact ctgggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc 600
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtct acaccaacct ctgcaaattc 660
 actgagtga tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa 720
 attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct 780
 ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc 840
 ccagcccct cctccctcag acccaggagt ccagaccccc cagcccctcc tccctcagac 900
 ccaggagtcc agcccctcct ccctcagacc caggagtcca gacccccag cccctcctcc 960
 ctcagaccca ggggtccagg cccccaaccc ctcctccctc agactcagag gtccaagccc 1020
 ccaaccntc attccccaga cccagaggtc cagggtcccag cccctcntcc ctcagaccca 1080
 gcggtccaat gccacctaga ctntccctgt acacagtgc cccttggtggc acgttgacct 1140
 aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt 1200
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1248

<210> 172
 <211> 159
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(159)
 <223> Xaa = Any Amino Acid

<400> 172
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1 5 10 15

60

Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
 20 25 30
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
 35 40 45
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
 50 55 60
 Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
 65 70 75 80
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
 85 90 95
 Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
 100 105 110
 Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
 115 120 125
 Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
 130 135 140
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 145 150 155

<210> 173
 <211> 1265
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1265)
 <223> n = A,T,C or G

<400> 173
 ggcagcccgc actcgcagcc ctggcaggcg gcaactgggtca tggaaaacga attgttctgc 60
 tcggggcgctcc tgggtgcatcc gcagtggggtg ctgtcagccg cacactgttt ccagaactcc 120
 tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg 180
 gtggaggcca gcctctccgt acggcaccga gactacaaca gacccttgct cgctaacgac 240
 ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc 300
 attgcttctgc agtgccttac cgcggggaac tcttgccctg tttctggctg gggctctgctg 360
 gcgaacgggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg 420
 cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga 480
 acgtgtcggg ggtgtctgag gaggtctgca gtaagctcta tgaccgctg taccacccca 540
 gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggg gactctgggg 600
 ggcccctgat ctgcaacggg tacttgacgg gccttggtgtc tttcggaata gcccgtgtg 660
 gccaaagtgg cgtgccagggt gtctacacca acctctgcaa attcactgag tggatagaga 720
 aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac 780
 atcctgcgga aggaattcag gaatatctgt tcccagcccc tcttccctca ggcccaggag 840
 tccaggcccc cagcccctcc tccctcaaac caagggtaca gatccccagc ccctcctccc 900
 tcagaccag gagtccagac ccccagccc ctctccctc agaccagga gtccagcccc 960
 tcctccntca gaccaggag tccagacccc ccagcccctc ctccctcaga cccagggggt 1020
 gagggcccca acccctcctc ctccagagtc agaggtocaa gcccacaacc cctcgttccc 1080
 cagaccaga ggttnnaggtc ccagcccctc ttccntcaga ccagnggtc caatgccacc 1140
 tagattttcc ctgnacacag tgccccttg tggngangttg acccaacctt accagttggt 1200
 ttttcatttt tngtcccttt cccctagatc cagaaataaa gttaaagaga nngcaaaaa 1260
 aaaaa 1265

<210> 174
 <211> 1459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1459)
 <223> n = A,T,C or G

<400> 174

ggtcagccgc	acactgtttc	cagaagttag	tgcagagctc	ctacaccatc	gggctgggccc	60
tgcacagtct	tgaggccgac	caagagccag	ggagccagat	ggtggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgctc	atcaagttgg	180
acgaatccgt	gtccgagtct	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcctta	240
ccgcggggaa	ctcttgctc	gtttctggct	ggggtctgct	ggcgaacggt	gagctcacgg	300
gtgtgtgtct	gccctcttca	aggaggctct	ctgcccagtc	gcgggggctg	acccagagct	360
ctgcgtccca	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tgggtgtctga	420
ngagggtctgc	antaagctct	atgacccgct	gtaccacccc	ancatgttct	gcgcggcgcg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
cagggaaagg	tggagaagg	ggagacagag	acacacaggg	ccgcatggcg	agatgcagag	600
atggagagac	acacagggag	acagtgacaa	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaagga	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcatggggcc	tgagggcggt	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtgcattt	atgcatacgt	900
tttatgcatt	catgatatac	ctttgttga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaaat	tgttgcaact	ctcctaaaat	ttttctgatg	tgttttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaacagg	gttgttcaag	ggtcaactgt	1080
gtacccagag	ggaaacagtg	acacagattc	atagaggtga	aacacgaaga	gaaacaggaa	1140
aaatcaagac	tctacaaaga	ggctgggcag	ggtggctcat	gcctgtaatc	ccagcacttt	1200
gggaggcgag	gcaggcagat	cacttgaggt	aaggagttca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatgggtgc	aggcgccctgt	1320
aatcccagct	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagagggt	1380
gaagtgagtt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaa					1459

<210> 175
 <211> 1167
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1167)
 <223> n = A,T,C or G

<400> 175

gcgcagccct	ggcaggcgcc	actggtcatg	gaaaacgaat	tgttctgctc	gggcgtcctg	60
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccacaga	gtacaacaga	ctcttgctcg	ctaacgacct	catgctcatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatacagcat	tgcttcgcag	300
tgccctaccg	cggggaaact	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgctgcaactg	cgtgaacgtg	tcgggtggtg	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgcgc	gcggaggggca	agaccagaag	480
gactcctgca	acggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgctg	cagggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccca	aatacatcct	gcggaangaa	ttcaggaata	tctgttccca	720
gcccctcctc	cctcaggccc	aggagtccag	gccccagcc	cctcctccct	caaaccagg	780
gtacagatcc	ccagcccctc	ctccctcaga	cccaggagtc	cagaccccc	agcccctcnt	840
ccntcagacc	caggagtcca	gcccctcctc	cntcagacgc	aggagtccag	acccccagc	900

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ccntcntccg tcagaccagc ggggtgcaggc ccccaacccc tcntccntca gagtcagagg 960
tccaagcccc caaccctcgc ttccccagac ccagagggtnc aggtcccagc ccctcctccc 1020
tcagaccagc cgggtccaatg ccacctagan tntccctgta cacagtgcgc ccttggtggca 1080
ngttgaccca accttaccag ttggtttttc attttttgtc cctttcccct agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa 1167

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<210> 176
<211> 205
<212> PRT
<213> Homo sapien

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<220>
<221> VARIANT
<222> (1)...(205)
<223> Xaa = Any Amino Acid

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<400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
1 5 10 15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
20 25 30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
35 40 45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
50 55 60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65 70 75 80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
85 90 95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100 105 110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
115 120 125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
130 135 140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145 150 155 160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
165 170 175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
180 185 190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
195 200 205

```

```

<210> 177
<211> 1119
<212> DNA
<213> Homo sapien

```

```

<400> 177
gcgcaactcgc agccctggca ggcggcactg gtcattggaaa acgaattgtt ctgctcgggc 60
gtcctgggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctctacacc 120
atcgggctg gctgcacag tcttgaggcc gaccaagagc caggagacca gatgggtggag 180
gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300
tcgcagtgcc ctacgcggg gaactcttgc ctcgtttctg gctggggtct gctggcgaaac 360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420
caaccctggc agggttgtac catttcggca acttccagtg caaggacgtc ctgctgcac 480

```

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ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgac aactagccag 540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720
tgacctacag aggtgagga tcatatagct cttcaaggat gctgggtactc ccctcacaaa 780
ttcattttctc ctggtttagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca 840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg 900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca 960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg 1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc 1080
ttaataaaca gaagctgtga tgtaaaaaa aaaaaaaaa 1119

```

<210> 178

<211> 164

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1)...(164)

<223> Xaa = Any Amino Acid

<400> 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1      5      10      15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
      20      25      30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
      35      40      45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
      50      55      60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
      65      70      75      80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
      85      90      95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
      100     105     110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
      115     120     125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
      130     135     140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
      145     150     155     160
Pro Gly Thr Leu

```

<210> 179

<211> 250

<212> DNA

<213> Homo sapien

<400> 179

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct 120
gccaggcaact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga 180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa 240
aaaaaaaaa 250

```

64 .

<210> 180
 <211> 202
 <212> DNA
 <213> Homo sapien

<400> 180
 actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca 60
 tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120
 ctctgtact cggaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc 180
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181
 <211> 558
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(558)
 <223> n = A,T,C or G

<400> 181
 tccytttgkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60
 aatgttttagg cagtgttagt aatttcytcg taatgattct gttattactt tcctnattct 120
 ttattctctt ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240
 aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300
 ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt ggggaagccaa 360
 attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
 aaaaacagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540
 caaaaaaaaa aaaaaaaaaa 558

<210> 182
 <211> 479
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(479)
 <223> n = A,T,C or G

<400> 182
 acagggwttk grggatgcta agscccorga rwtggtttga tccaacctg gcttwttttc 60
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120
 cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcaggccctg 180
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
 ctaagggttaa actttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
 tactmttcta agtcctcttc cagcctcact kkgagtcctm cytgggggtt gataggaant 360
 ntctcttggc tttctcaata aartctctat ycatctcatg ttaatttgg tacgcatara 420
 awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183
 <211> 384
 <212> DNA
 <213> Homo sapien

65

<400> 183
 aggcgggagc agaagctaaa gccaaagccc aagaagagtgc gcagtgccag cactgggtgcc 60
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg ctccagtgc 120
 ggtgccagcc tgaccgccac tctcacattt gggtctctcg ctggccttgg tggagctggt 180
 gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat 240
 tgtaatacct gccagtcttt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca 300
 cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt 360
 gccatttcaa aaaaaaaaaa aaaa 384

<210> 184

<211> 496

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(496)

<223> n = A,T,C or G

<400> 184
 accgaattgg gaccgctggc ttataagcga tcatgttynt ccrgtatcac ctcaacgagc 60
 agggagatcg agtctatacg ctgaagaaat ttgaccgat gggacaacag acctgctcag 120
 cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga 180
 aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac 240
 tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact ctccgactg 300
 tgagccctga tgcccttttg ccagccatac tctttggcat ccagtctctc gtggcgattg 360
 attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt 420
 tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst 480
 taaaaaaaaa aaaaaa 496

<210> 185

<211> 384

<212> DNA

<213> Homo sapien

<400> 185
 gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc 60
 caagtatcyt ggcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc 120
 aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct 180
 gggcacacc tccctggggc caggcgggca cctgcgtctc ccagtatgcc aactggctgg 240
 tggtgctgct cctcgtcatc ttcctgctcg tggccaacat cctgctggtc aacttgctca 300
 ttgccatgtt cagttacaca ttcggcaaaag tacagggcaa cagcgatctc tactgggaag 360
 gcgcagcgtt accgcctcat ccgg 384

<210> 186

<211> 577

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(577)

<223> n = A,T,C or G

<400> 186
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
 tnccatcgtc atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt 120
 ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctgggtc tgtcttcgc 180

66

tgggtgtgaa	aggatctccc	agaaggagt	ctcgatcttc	cccacacttt	tgatgacttt	240
attgagtcga	ttctgcatgt	ccagcaggag	gttgtagcag	ctctctgaca	gtgaggtcac	300
cagccctatc	atgccgttga	mcgtgccgaa	garcaccgag	ccttgtgtgg	gggkkgag	360
ctcaccacga	ttctgcatta	ccagagagcc	gtggcaaaa	acattgacaa	actcggccag	420
gtggaaaaag	amcamctcct	ggargtgctn	gccgctcctc	gtcmgttggt	ggcagcgctw	480
tccttttgac	acacaaaaca	gttaaaggca	ttttcagccc	ccagaaantt	gtcatcatcc	540
aagatntcgc	acagcactna	tccagttggg	attaaat			577

<210> 187
 <211> 534
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(534)
 <223> n = A,T,C or G

aacatcttcc	tgtataatgc	tgtgtaatat	cgatccgatn	ttgtctgstg	agaatycatw	60
actkggaaaa	gmaacattaa	agcctggaca	ctggtattaa	aattcacaat	atgcaacact	120
ttaaacagtg	tgtcaatctg	ctcccyynac	tttgtcoatc	ccagtctggg	aakaagggta	180
tgcctatttc	acacctgtta	aaagggcgct	aagcattttt	gattcaacat	cttttttttt	240
gacacaagtc	cgaaaaaagc	aaaagtaaac	agttatyaat	ttgttagcca	attcactttc	300
ttcatgggac	agagccatyt	gatttaaaaa	gcaaattgca	taatattgag	cttygggagc	360
tgatatttga	gcggaagagt	agcctttcta	cttcaccaga	cacaactccc	tttcatattg	420
ggatgttnac	naaagtwatg	tctctwacag	atgggatgct	tttgtggcaa	ttctgttctg	480
aggatctccc	agtttattta	ccacttgcac	aagaaggcgt	tttcttcttc	aggc	534

<210> 188
 <211> 761
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(761)
 <223> n = A,T,C or G

agaaaccagt	atctctnaaa	acaacctctc	ataccttggt	gacctaat	ttgtgtcggt	60
tgtgtgtgcg	cgcataattat	atagacaggc	acatcttttt	tacttttgta	aaagcttatg	120
cctcttttgg	atctatatct	gtgaaagttt	taatgatctg	ccataatgtc	ttggggacct	180
ttgtcttctg	tgtaaatggt	actagagaaa	acacctatnt	tatgagtcaa	tctagttngt	240
tttattcgac	atgaaggaaa	ttccagatn	acaacactna	caaaactctc	ctkgackarg	300
ggggacaaa	aaaagcaaaa	ctgamcataa	raaacaatwa	cctgggtgaga	arttgcataa	360
acagaaatwr	ggtagtatat	tgaarnacag	catcattaaa	rmgttwtktt	wttctccott	420
gcaaaaaaca	tgtacngact	tcccgttgag	taatgccaag	ttgttttttt	tatnataaaa	480
cttgcccttc	attacatggt	tnaaagtggg	gtgggtggcc	aaaatattga	aatgatggaa	540
ctgactgata	aagctgtaca	aataagcagt	gtgcctaaca	agcaacacag	taatgttgac	600
atgcttaatt	cacaaatgct	aatttcatta	taaatgtttg	ctaaaataca	ctttgaacta	660
tttttctgt	ttcccagagc	tgagatntta	gattttatgt	agtatnaagt	gaaaaantac	720
gaaataata	acattgaaga	aaaananaaa	aaanaaaaaa	a		761

<210> 189
 <211> 482
 <212> DNA
 <213> Homo sapien

67

<220>
 <221> misc_feature
 <222> (1)...(482)
 <223> n = A,T,C or G

<400> 189
 tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60
 caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120
 aagccgcctg ctgccttctc tgtctgtctc ctgggtgcagg cacatgggga gaccttcccc 180
 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240
 tgataggcac aggccaccg gtacagacc ctcggctcct gacaggtnga tttcgaccag 300
 gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc 360
 aaatttggtc ngtcattngaa ngggcanttt tccaanttng gctnnggtctt ggtacncttg 420
 gttcggccca gctccnctgc caaaaantat tcaccennct ccnaattgct tgcnggnccc 480
 cc 482

<210> 190
 <211> 471
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(471)
 <223> n = A,T,C or G

<400> 190
 tttttttttt ttttfaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg 60
 aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtntctca 120
 aatgtctggg caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180
 cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt 240
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300
 tgaaaaaattt catgtatgca atccaaccaa agaacttnat tgggtgatcat gantnctcta 360
 ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaaanaa 420
 tctgtaattn anttcaacct ccgtacngaa aaatnttntt tatacactcc c 471

<210> 191
 <211> 402
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(402)
 <223> n = A,T,C or G

<400> 191
 gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60
 gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120
 attcttcacc agtcacatct tctaggacct ttttggtatc agttagtata agctcttcca 180
 ctctctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg 240
 ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc 300
 ctttgtgcat ccatttttaa tatacttaat agggcattgk tncaactagg taaattctgc 360
 aagagtcate tgtctgcaaa agttgcgtta gtatactctgc ca 402

<210> 192
 <211> 601

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(601)
<223> n = A,T,C or G

<400> 192
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact 60
ggtctacccc acatgggagc agcatgccgt agntatataa ggctattccc tgagtcagac 120
atgcytyttt gaytaccgtg tgccaagtgc tgggtattct yaacacacyt ccatcccgyt 180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc 240
acgagacact tgaaagggtg aacaaagcga ytcttgccatt gctttttgtc cctccggcac 300
cagttgtcaa tactaaccog ctggtttgcc tccatcacat ttgtgatctg tagctctgga 360
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcarg tcttgggtgcc 420
tgttgatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac 480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag 540
cctcgatgta gccggccagc gccaaaggcag gcgccgtgag ccccaccagc agcagaagca 600
g 601

<210> 193
<211> 608
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(608)
<223> n = A,T,C or G

<400> 193
atacagccca natcccacca cgaagatgag cttgttgact gagaacctga tgcggtcact 60
ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt 120
cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg 180
tkaagtgcag gaagaggctg accacctogc ggtccaccag gatgcccagc tgtgccccgac 240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc 300
agaaccttcc gcctgttctc tggcgtaacc tgcagctgct gccgctgaca ctcggcctcg 360
gaccagcgga caaacggcrt tgaacagccg cacctcacgg atgccagtg tgcgcgcctc 420
caggammgsc accagcgtgt ccaggtcaat gtcggtgaag ccctccgcgg gtrattggcg 480
ctgcagtgtt tttgtcgatg ttctccaggc acaggtggc cagctgcggg tcatcgaaga 540
gtcgcgcctg cgtgagcagc atgaaggcgt tgcgggctcg cagttcttct tcaggaaactc 600
cacgcaat 608

<210> 194
<211> 392
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

<400> 194
gaacggctgg accttgccctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt 60
ccagtcgcag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc 120
tccgcctcaa tgagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg 180

tttgatttta	ottgggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgcctgtt	aagttgtata	aaagtaggtg	attctgtatt	300
taaagaaaat	attactgtta	catatactgc	ttgcaatttc	tgtattttatt	gktnctstgg	360
aaataaatat	agttattaaa	ggttgtcant	cc			392

<210> 195
 <211> 502
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 195						
ccsttkgagg	ggtkaggkyc	cagttyccga	gtggaagaaa	caggccagga	gaagtgcgtg	60
ccgagctgag	gcagatgttc	ccacagtgc	ccccagagcc	stgggstata	gtytctgacc	120
cctcncaagg	aaagaccacs	ttctggggac	atgggctgga	gggcaggacc	tagaggcacc	180
aagggaaggc	ccattccgg	ggstgttccc	cgaggaggaa	gggaaggggc	totgtgtgcc	240
ccccasgagg	aagaggccct	gagtcctggg	atcagacacc	ccttcacgtg	tatccccaca	300
caaatgcaag	ctcaccaagg	tcccctctca	gtccccttcc	stacaccctg	amcgggccact	360
gscscacacc	caccagagc	acgccacccg	ccatggggar	tgtgctcaag	gartcgcnng	420
gcarcgtgga	catctngtcc	cagaaggggg	cagaatctcc	aatagangga	ctgarcmstt	480
gctnanaaaa	aaaaanaaaa	aa				502

<210> 196
 <211> 665
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(665)
 <223> n = A,T,C or G

<400> 196						
ggttacttg	tttcattgcc	accacttagt	ggatgtcatt	tagaaccatt	ttgtctgctc	60
cctctggaag	ccttgccgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
wagctgtttk	gagttgatts	gcaccactgc	accacaact	tcaatatgaa	aacyawttga	180
actwatattat	tatcttgatga	aaagtataac	aatgaaaatt	ttgttcatac	tgtattkatc	240
aagtatgatg	aaaagcaawa	gatatatatt	cttttattat	gttaaattat	gattgccatt	300
attaatcggc	aaaatgtgga	gtgtatgttc	ttttcacagt	aatatatgcc	ttttgtaact	360
tcacttggtt	attttatgt	aaatgartta	caaaattctt	aatttaagar	aatggatgt	420
watatttatt	tcattaattt	ctttcctkgt	ttacgtwaat	tttgaaaaga	wtgcatgatt	480
tcttgacaga	aatcgatctt	gatgctgtgg	aagtagtttg	accacatcc	ctatgagttt	540
ttcttagaat	gtataaagg	tgtagcccat	cnaacttcaa	agaaaaaat	gaccacatac	600
tttgcaatca	ggctgaaatg	tggcatgctn	ttctaattcc	aactttataa	actagcaaan	660
aagtg						665

<210> 197
 <211> 492
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(492)

<223> n = A,T,C or G

<400> 197

tttntttttt	ttttttttgc	aggaaggatt	ccattttattg	tggatgcatt	ttcacaatat	60
atgtttattg	gagcgatcca	ttatcagtga	aaagtatcaa	gtgtttataa	natttttagg	120
aaggcagatt	cacagaacat	gctngtongc	ttgcagtttt	acctcgtana	gatnacagag	180
aattatagtc	naaccagtaa	acnaggaatt	tacttttcaa	aagattaaat	ccaaactgaa	240
caaaattcta	ccctgaaact	tactccatcc	aaatattgga	ataanagtca	gcagtgatac	300
attctcttct	gaactttaga	ttttctagaa	aaatatgtaa	tagtgatcag	gaagagctct	360
tgttcaaaag	tacaacnaag	caatgttccc	ttaccatagg	ccttaattca	aactttgatc	420
catttcactc	ccatcacggg	agtcaatgct	acctgggaca	cttgatattt	gttcatnctg	480
ancntggctt	aa					492

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(478)

<223> n = A,T,C or G

<400> 198

tttnttttgn	atttcantct	gtannaanta	ttttcattat	gtttattana	aaaatatnaa	60
tgnttccacn	acaaatcatn	ttacntnagt	aagaggccan	ctacattgta	caacatacac	120
tgagtatatt	ttgaaaagga	caagttttaa	gtanacncat	attgccganc	atancacatt	180
tatacatggc	ttgattgata	tttagcacag	canaaactga	gtgagttacc	agaaanaaat	240
natatatgtc	aatcngattt	aagatacaaa	acagatccta	tggtagatan	catcntgtag	300
gagttgtggc	tttatgttta	ctgaaagtca	atgcagttcc	tgtacaaaga	gatggccgta	360
agcattctag	tacctctact	ccatgggtta	gaatcgtaca	cttatgttta	catatgtnc	420
gggtaagaat	tgtgttaagt	naanttatgg	agaggtccan	gagaaaaatt	tgatncaa	478

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 199

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtcc	tgatcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaatctatt	cctacttgta	cggactttga	180
agtgattcag	tttcctctac	ggatgagaga	ctggctcaag	aatatcctca	tgcagcttta	240
tgaagccnac	tctgaacacg	ctggttatct	nagatgagaa	ncagagaaat	aaagtcnaga	300
aaatttacct	ggangaaaag	aggctttngg	ctggggacca	tcccattgaa	ccttctctta	360
anggacttta	agaanaaaact	accacatgtn	tgtngtatcc	tgggtgccngg	ccgtttantg	420
aacntngacn	ncacccttnt	ggaatanant	cttgacngcn	tcctgaactt	gctcctctgc	480
ga						482

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(270)
 <223> n = A,T,C or G

<400> 200
 cgccgcgaag tgcaactcca gctggggccg tgcggacgaa gattctgcc a gcagttggtc 60
 cgactgcgac gacggcgccg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120
 aaggctgagc tgacgccgca gaggtcgtgt cacgtccac gaccttgacg ccgtcgggga 180
 cagccggaac agagcccggg gaangcggga ggcctcgggg agcccctcgg gaaggcgccg 240
 ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201
 <211> 419
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(419)
 <223> n = A,T,C or G

<400> 201
 tttttttttt ttttggaaatc tactgcgagc acagcaggtc agcaacaagt ttatttttgca 60
 gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg 120
 ttgattgggt tgtcttttatg gggcggggtt ggggtagggg aaancgaagc anaantaaca 180
 tggagtgggt gcaacctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg 240
 tctgtgacgg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag 300
 tccactgtnt ctggaggagg attagggttt cttgccaana tccaancaa atccacntga 360
 aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca 419

<210> 202
 <211> 509
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 202
 tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120
 gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaattnaa 180
 tacnncnaaa aatcaaaaat ataentntct ttcagcaaac ttngttacat aaattaaaaa 240
 aatatatacg gctgggtggt tcaaagtaca attatcttaa cactgcaaac atnttttnaa 300
 ggaactaaaa taataaaaaa cactnccgca aaggttaag ggaacaacaa attcntttta 360
 caacancnnc nattataaaa atcatatctc aaatccttag ggaatatata cttcacacng 420
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480
 caatggnaat ncncncncncc tggactagt 509

<210> 203
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

<400> 203
 tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttatttttact 60
 tacacatatt ttttttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac 120
 taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt 180
 gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240
 atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300
 gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360
 agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca ttttcttacc 420
 tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg 480
 tccatttttag tcaactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt 540
 attcaaaagc taatataaga tttttcacat actcatctt ctg 583

<210> 204
 <211> 589
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(589)
 <223> n = A,T,C or G

<400> 204
 ttttttttnt tttttttttt ttttttntct ttcttttttt ttganaatga ggatcgagtt 60
 tttcactctc tagatagggc atgaagaaaa ctcatctttc cagcttttaa ataacaatca 120
 aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc 180
 tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat 240
 tgagagggtt ttcttctcta tttacacata tttttccatg tgaatttgta tcaaaccctt 300
 attttcatgc aaactagaaa ataattgtnt cttttgcata agagaagaga acaatatnag 360
 cattacaaaa ctgctcaaat tggttggttaa gnttatccat tataattagt tnggcaggag 420
 ctaatacaaa tcacattttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc 480
 aaaataatta aagggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat 540
 ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg 589

<210> 205
 <211> 545
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(545)
 <223> n = A,T,C or G

<400> 205
 tttttntttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat 60
 agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120
 tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat 180
 ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt 240
 aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat 300
 atgggggtgc actggtaaac caacacattc tgaaggatac attacttagt gatagattct 360
 tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt 420
 aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg 480

aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540
aacc 545

<210> 206
<211> 487
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(487)
<223> n = A,T,C or G

<400> 206
tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttgggtcattt 60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120
caatttataa atgtaagggt ccattattga gtanatatat tcctccaaga gtggatgtgt 180
cccttctccc accaactaat gaancagcaa cattagtta attttattag tagatnatac 240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt 360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag 420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480
ttcaaaa 487

<210> 207
<211> 332
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(332)
<223> n = A,T,C or G

<400> 207
tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa 60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact 120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana 180
atctttgcat gcagaggagg taaaaggat tggattttca cagagggaana acacagcgca 240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg 300
aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208
<211> 524
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(524)
<223> n = A,T,C or G

<400> 208
agggcgtggt gcggaggggc ttactgtttt gtctcagtaa caataaatac aaaaagactg 60
gttggttcc ggcccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat 120
tttaaaggac atggagcttg tcacaatgac acaatgtcac agtgtgaagg gcacactcac 180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact 240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa 300

gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc	360
atgagcccag acactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc	420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa	480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga	524

<210> 209
 <211> 159
 <212> DNA
 <213> Homo sapien

<400> 209	
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg	60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca	120
caaaggactc tcgacccaaa ctgcccacaga cctctctca	159

<210> 210
 <211> 256
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(256)
 <223> n = A,T,C or G

<400> 210	
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc	60
actgaatttc ttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta	120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat	180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca	240
ccaggatgct aatca	256

<210> 211
 <211> 264
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(264)
 <223> n = A,T,C or G

<400> 211	
acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg	60
actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt	120
atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga	180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga	240
aaaaaaggag caaatgagaa gcct	264

<210> 212
 <211> 328
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(328)
 <223> n = A,T,C or G

<400> 212
 acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa 60
 ggattttaatg ttgtctcagc ttgggcaqtt cagttaggac ctaaggatgc cagccggcag 120
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180
 ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240
 ccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300
 ttttttttct ctttattcct ttgtcaga 328

<210> 213

<211> 250

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(250)

<223> n = A,T,C or G

<400> 213
 acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120
 cattatgcca aagganatat acattttcaat tctccaaact tcttcctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct 240
 tctcatcggt 250

<210> 214

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(444)

<223> n = A,T,C or G

<400> 214
 acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag 60
 gattttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcag 120
 tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccgccagt 180
 tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac 240
 ccctacgact ctttactctc tggagagggc cagtgggtgt agctataagc ttggccacat 300
 ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag 360
 agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt 420
 actttgctct ccctaataata cctc 444

<210> 215

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(366)

<223> n = A,T,C or G

<400> 215
 acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60

taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgcca	aagganatat	acatttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatat	gcatgaacct	gctgataagc	catgttgaga	aacaaataic	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccagg	ttccaaccaa	ggtggaaatc	tcctatactt	360
ggtgcc						366

<210> 216
 <211> 260
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(260)
 <223> n = A,T,C or G

<400> 216	
ctgtataaac	agaactccac
tgcanagggg	agggccgggc
caggagaatc	tccgcttgct
caagacaggg	gcctaaggag
ggtctccaca	ctgctnntaa
gggctnttnc	atTTTTTTat
taataaaaag	tnnaaaaggc
ctcttctcaa	ctTTTTTccc
ttnggctgga	aaatttaaaa
atcaaaaatt	tcctnaagtt
ntcaagctat	catatatact
ntatcctgaa	aaagcaacat
aattcttcct	tccctccttt
	260

<210> 217
 <211> 262
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(262)
 <223> n = A,T,C or G

<400> 217	
acctacgtgg	gtaagtttan
aaatgttata	atttcaggaa
naggaacgca	tataattgta
tcttgcoctat	aattttctat
tttaataagg	aaatagcaaa
ttgggggtggg	gggaatgtag
ggcattctac	agtttgagca
aaatgcaatt	aaatgtggaa
ggacagcact	gaaaaatttt
atgaataatc	tgtatgatta
tatgtctcta	gagtagattt
ataattagcc	acttacccta
atataccttca	tgcttgtaaa
gt	
	262

<210> 218
 <211> 205
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(205)
 <223> n = A,T,C or G

<400> 218	
accaaggtgg	tgcatcaccg
gaantggatc	aangacacca
tcgtggccaa	cccctgagca
cccctatcaa	ctcccttttg
tagtaaaactt	ggaaccttgg
aaatgaccag	gccaagactc
aggcctcccc	agttctactg
acctttgtcc	ttangntna
ngtccagggt	tgctaggaaa
anaaatcagc	agacacaggt
gtaaa	
	205

<210> 219

77

<211> 114
 <212> DNA
 <213> Homo sapien

<400> 219
 tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gcccacatcca 60
 accacgaagt tgattttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220
 <211> 93
 <212> DNA
 <213> Homo sapien

<400> 220
 actagccagc acaaaaggca gggtagcctg aattgctttt tgctctttac atttctttta 60
 aaataagcat ttagtgctca gtccctactg agt 93

<210> 221
 <211> 167
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(167)
 <223> n = A,T,C or G

<400> 221
 actangtgca ggtgcgacaca aatatttgct gatattccct tcatcttgga ttocatgagg 60
 tcttttgccc agcctgtggc totactgtag taagtttctg ctgatgagga gccagnatgc 120
 cccccactac cttccctgac gctccccana aatcacccaa cctctgt 167

<210> 222
 <211> 351
 <212> DNA
 <213> Homo sapien

<400> 222
 agggcggtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60
 gttcttcacc tgtcccccaa tccttaaaaag gccatactgc ataaagtcaa caacagataa 120
 atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180
 ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240
 taggtgagca tgattagaga gcttgtagggt tgcttttaca tatatctggc atatttgagt 300
 ctcgtatcaa aacaatagat tggtaaagggt ggtattattg tattgataag t 351

<210> 223
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(383)
 <223> n = A,T,C or G

<400> 223
 aaaacaaaca acaaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60
 tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120

ttaaaaatgtc	tgtgccaaaa	ttttgtat	tatttggaga	cttcttatca	aaagtaatgc	180
tgccaaagga	agtctaagga	attagtagtg	ttcccmcac	ttgtttggag	tgtgctattc	240
taaaagattt	tgatttcctg	gaatgacaat	tatatittaa	ctttggtggg	ggaaanagtt	300
ataggaccac	agtcttcact	tctgatactt	gtaaattaat	cttttattgc	acttgttttg	360
accattaagc	tatatgttta	aaa				383

<210> 224
 <211> 320
 <212> DNA
 <213> Homo sapien

<400> 224						
ccccgaagg	cttcttgta	gaaaatagta	cagttacaac	caataggaac	aacaaaaaga	60
aaaagtgtt	gacattgtag	tagggagtgt	gtaccoccta	ctcccatca	aaaaaaaaat	120
ggatacatgg	ttaaaggata	raagggaat	attttatcat	atgttctaaa	agagaaggaa	180
gagaaaatac	tactttctcr	aaatggaagc	ccttaaaggt	gctttgatac	tgaaggacac	240
aaatgtggcc	gtccatcctc	ctttaragtt	gcatgacttg	gacacggtaa	ctgttgcaagt	300
tttaractcm	gcattgtgac					320

<210> 225
 <211> 1214
 <212> DNA
 <213> Homo sapien

<400> 225						
gaggactgca	gcccgcactc	gcagccctgg	caggcgccac	tggtcatgga	aaacgaattg	60
ttctgctcgg	gcgtcctggt	gcatccgcag	tgggtgctgt	cagccgcaca	ctgtttccag	120
aaactctaca	ccatcgggct	gggcctgcac	agtcttgagg	ccgaccaaga	gccaggagac	180
cagatggtgg	agccagcct	ctccgtacgg	caccagaggt	acaacagacc	cttgctcgct	240
aacgacctca	tgctcatcaa	gttggaagaa	tccgtgtccg	agtctgacac	catccggagc	300
atcagcattg	cttcgcagtg	ccctaccgcg	gggaactctt	gcctcgtttc	tggtctgggt	360
ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	tgaacgtgtc	ggtggtgtct	420
gaggaggtct	gcagtaagct	ctatgaccgg	ctgtaccacc	ccagcatggt	ctgcgcgggc	480
ggaggggcaag	accagaagga	ctcctgcaac	ggtgactctg	ggggggccct	gatctgcaac	540
gggtacttgc	agggccttgt	gtctttcgga	aaagccccgt	gtggccaagt	tggcgtgcca	600
ggtgtctaca	ccaacctctg	caaattcact	gagtggatag	agaaaaccgt	ccaggccagt	660
taactctggg	gactgggaac	ccatgaaatt	gacccccaaa	tacatcctgc	ggaagggaatt	720
caggaatatc	tggtcccagc	ccctcctccc	tcaggcccag	gagtccaggc	ccccagcccc	780
tcctccctca	aaccaagggt	acagatcccc	agccctcctc	ccctcagacc	caggagtcca	840
gacccccccag	cccctcctcc	ctcagaccca	ggagtccagc	ccctcctccc	tcagacccag	900
gagtccagac	ccccagccc	ctcctccctc	agaccaggg	gtccaggccc	ccaaccctc	960
ctcctcaga	ctcagaggtc	caagccccca	accctcctt	ccccagaccc	agaggtccag	1020
gtcccagccc	ctcctccctc	agaccagcg	gtccaatgcc	acctagactc	tcctgtaca	1080
cagtgcctcc	ttgtggcacg	ttgacccaac	cttaccagtt	ggtttttcat	ttttgtccc	1140
tttcccctag	atccagaaat	aaagtctaag	agaagcgcaa	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaa					1214

<210> 226
 <211> 119
 <212> DNA
 <213> Homo sapien

<400> 226						
accagtatg	tcagggaga	cggaacccca	tgtgacagcc	cactccacca	gggttcccaa	60
agaacctggc	ccagtcataa	tcattcatcc	tgacagtggc	aataatcacg	ataaccagt	119

<210> 227
 <211> 818

<212> DNA

<213> Homo sapien

<400> 227

acaattcata	gggacgacca	atgaggacag	ggaatgaacc	cggctctccc	ccagccctga	60
tttttgctac	atatggggtc	ccttttcatt	ccttgcaaaa	acactgggtt	ttctgagaac	120
acggacggtt	cttagcacia	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcttc	ctctggagga	aaggtggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgctccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttcct	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaaggggtg	caccctcagc	agagaagccg	agagcttaac	tctggctcgt	tccagagaca	480
acctgtcggc	tgtcttgagg	tgcgccagc	ccttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggtc	720
caagaggata	tgaggactgt	ctcagcctgg	ccttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818

<210> 228

<211> 744

<212> DNA

<213> Homo sapien

<400> 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaacga	gcctcctcct	tggaagatgg	aagaccgtgt	120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
tgtcgggtgc	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	cgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctgggtga	cagtgaccgc	540
ccgtgggtatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttgggggttg	600
ttcttttcgt	taatgttctc	ctgtgttgtc	agctgtcttc	atttcctggg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttcactctg	aagtagctgg	tggt				744

<210> 229

<211> 300

<212> DNA

<213> Homo sapien

<400> 229

cgagtctggg	ttttgtctat	aaagtttcat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgacgggttg	ttgtttttta	attattattg	ttagaaacgt	caccacacag	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagctc	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

<210> 230

<211> 301

<212> DNA

<213> Homo sapien

<400> 230

cagcagaaca	aatacaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
------------	------------	------------	------------	------------	------------	----

gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg 120
 caatataaag tcctgggttca cactcaggaa cgagagctga cccagttaag ggagaagttg 180
 cgggaaggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg 240
 gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgaccac 300
 g 301

<210> 231
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 231
 gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcatttttagc 60
 caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat 120
 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240
 tttttttgtg gacatgccat ccattttctgt caggatctgg ttgatgactc ggtcagcagc 300
 c 301

<210> 232
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 232
 agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagttctcc ttcaagtgtt 60
 ggcgacagcg gggcttctcg attctggaat ataactttgt gtaaattaac agccacctat 120
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtccgtgtcca 180
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tctactgaaa tctggctaatt 240
 gctcttctgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
 g 301

<210> 233
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 233
 atgactgact tcccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag 60
 atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg 120
 cctagaagtt acagagcatc tagctggtgc gctggcaccc ctggcctcac acagactccc 180
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240
 tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300
 c 301

<210> 234
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 234
 aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60
 catttttatt atcatgatgc tttcttttgt ttctttttt cgtttttttc tttttctttt 120
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180
 cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgc 240
 ttgatcacca gcttaatggt cagatcatct gttcaatgg ctctcgtcagt atagttcttc 300
 t 301

81

<210> 235
 <211> 283
 <212> DNA
 <213> Homo sapien

<400> 235
 tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg 60
 aattccctca tcttttaggg aatcatttac cagggtttgga gaggattcag acagctcagg 120
 tgctttcact aatgtctctg aacttctgtc cctctttggt catggatagt ccaataaata 180
 atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatacaaca 240
 ttagggattc aaagaaatat tagatttaag ctcacactgg tca 283

<210> 236
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 236
 aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata 60
 aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg 120
 tcggagcagc atcattaata ccaagcagaa tgcgtaatat ataaatacaa tggatatatag 180
 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta 240
 aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300
 a 301

<210> 237
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 237
 cagtggtagt ggtggtggac gtggcggttg tcgtggtgcc ttttttggtg cccgtcacia 60
 actcaatttt tgttcgctcc tttttggcct ttccaattt gtccatctca attttctggg 120
 ccttggctaa tgccatcatg taggagtcct cagaccagcc atggggatca aacatatcct 180
 ttgggtagt ttgtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaactta 240
 gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctccctttatc 300
 t 301

<210> 238
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 238
 gggcagggtt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt 60
 gttcacagtt cagccccctg ctcaaaaaac caacggggcca gctaaggaga ggaggaggca 120
 ccttgagact tccggagtcg aggcctctcca gggttcccca gcccatcaat cattttctgc 180
 accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240
 gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300
 t 301

<210> 239
 <211> 239
 <212> DNA
 <213> Homo sapien

<400> 239
 ataagcagct aggggaattct ttatttagta atgtcctaac ataaaagttc acataactgc 60

ttctgtcaaa ccatgatact gagctttgtg acaacccaga aataactaag agaaggcaaa	120
cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac	180
attcagccag tgagtagagt gtgaatgcc aacatacacag tatacaggtc cttcaggga	239

<210> 240
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 240	
ggtcctaagt aagcagcagc ttccacattt taacgcaggt ttacgggtgat actgtccttt	60
gggatctgcc ctccagtga accttttaag gaagaagtgg gcccaagcta agttccacat	120
gctgggtgag ccagatgact tctgttccct ggtaactttc ttcaatgggg cgaatggggg	180
ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtaacttca ccctcctcac	240
gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc	300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241	
gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga	60
cctctttgga ggaaactcca gcagctatgt tgggtgtctct gaggggaatgc aacaaggctg	120
ctcctccatg tattggaaaa ctgcaaaactg gactcaactg gaaggaagtg ctgctgccag	180
tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct	240
tcctcctcct gtcatacggg ctctctcaag catcctttgt tgtcaggggc ctaaaaggga	300
g	301

<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242	
ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt	60
tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat	120
gtcttcaaga atatatcatt cctttttcac tagaaccat tcaaaatata agtcaagaat	180
cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta	240
taagtaccca aagttttata aatcaaaagc cctaatagata accattttta gaattcaatc	300
a	301

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243	
aggtaagtcc cagtttgaag ctcaaaagat ctgggtatgag cataggctca tcgacgacat	60
gggtggccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg	120
tgacgtgcag tcggactctg tggcccaagg gtatggctct ctggcatga tgaccagcgt	180
gctggtttgt ccagatggca agacagtaga agcagaggct gccacaggga ctgtaaccg	240
tcactaccgc atgttccaga aaggacagga gacgtccacc aatcccattg cttccatttt	300
t	301

<210> 244
 <211> 300
 <212> DNA

<213> Homo sapien

<400> 244

gctggtttgc	aagaatgaaa	tgaatgattc	tacagctagg	acttaacctt	gaaatggaaa	60
gtcatgcaat	cccatttgca	ggatctgtct	gtgcacatgc	ctctgtagag	agcagcattc	120
ccagggacct	tggaaacagt	tgacactgta	aggtgcttgc	tccccaagac	acatcctaaa	180
aggtgttgta	atggtgaaaa	cgtcttcctt	ctttattgcc	ccttcttatt	tatgtgaaca	240
actgtttgc	ttttgtgtat	cttttttaaa	ctgtaaagtt	caattgtgaa	aatgaatata	300

<210> 245

<211> 301

<212> DNA

<213> Homo sapien

<400> 245

gtctgagtat	ttaaaatggt	attgaaatta	tccccaacca	atgttagaaa	agaaagaggt	60
tatatactta	gataaaaaat	gaggtgaatt	actatccatt	gaaatcatgc	tcttagaatt	120
aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	cactcaatac	240
agctaataaa	atgaaagacc	taatttctaa	agcaattctt	tataatttac	aaagttttaa	300
g						301

<210> 246

<211> 301

<212> DNA

<213> Homo sapien

<400> 246

ggtctgtcct	acaatgcctg	cttcttgaaa	gaagtcggca	ctttctagaa	tagctaaata	60
acctgggctt	attttaaaga	actatttgta	gtcagattg	gttttcctat	ggctaaaata	120
agtgccttct	gtgaaaatta	aataaaacag	ttaattcaaa	gccttgatat	atgttaccac	180
taacaatcat	actaaatata	ttttgaagta	caaagtttga	catgctctaa	agtgacaacc	240
caaatgtgtc	ttacaaaaca	cgttcctaac	aaggatatgt	ttacactacc	aatgcagaaa	300
c						301

<210> 247

<211> 301

<212> DNA

<213> Homo sapien

<400> 247

aggtcctttg	gcagggctca	tggatcagag	ctcaaactgg	agggaaaggc	atttcgggta	60
gcctaagagg	gcgactggcg	gcagcacaac	caaggaaggc	aaggttggtt	ccccacgct	120
gtgtcctgtg	ttcaggtgcg	acacacaatc	ctcatgggaa	caggatcacc	catgcgctgc	180
ccttgatgat	caaggttggg	gcttaagtgg	attaaggag	gcaagttctg	ggttccttgc	240
cttttcaaac	catgaagtca	ggctctgtat	ccctcctttt	cctaactgat	attctaacta	300
a						301

<210> 248

<211> 301

<212> DNA

<213> Homo sapien

<400> 248

aggtccttgg	agatgccatt	tcagccgaag	gactcttctw	ttcggaagta	caccctcact	60
attaggaaga	ttcttagggg	taatttttct	gaggaaggag	aactagccaa	cttaagaatt	120
acaggaagaa	agtggtttgg	aagacagcca	aagaaataaa	agcagattaa	attgtatcag	180
gtacattcca	gcctgttggc	aactccataa	aaacatttca	gattttaatc	ccgaatttag	240

ctaagagac tggatTTTTg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300
c 301

<210> 249
<211> 301
<212> DNA
<213> Homo sapien

<400> 249
gtccagagga agcacctggg gctgaactag gcttgccctg ctgtgaactt gcacttggag 60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgccc 120
ccaggagac acagcagtga ctacagagctg gtcgcacact gtgcctccct cctcaccgcc 180
catcgtaatg aattatTTTg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt 300
a 301

<210> 250
<211> 301
<212> DNA
<213> Homo sapien

<400> 250
ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc 60
cttatcttta ttggcttgat aaacataatt atttctaaca ctactttatt tccagttgcc 120
cataagcaca tcagtacttt tctctggctg gaatagtaaa cttaaagtatg gtacatctac 180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta 240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300
a 301

<210> 251
<211> 301
<212> DNA
<213> Homo sapien

<400> 251
gccgaggtcc tacatttggc ccagtttccc cctgcacact ctccagggcc cctgcctcat 60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat 120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct 180
cattgggatac aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgaa 240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct 300
c 301

<210> 252
<211> 301
<212> DNA
<213> Homo sapien

<400> 252
gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgttg catttcctca 60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata 120
tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa 180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag taccctaaag 240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300
a 301

<210> 253
<211> 301
<212> DNA

<213> Homo sapien

<400> 253

ttccctaaga	agatgttatt	ttgttgggtt	ttgttcccc	tccatctcga	ttctcgtacc	60
caactaaaaa	aaaaaaataa	agaaaaaatg	tgctgcgttc	tgaaaaataa	ctccttagct	120
tggtctgatt	gttttcagac	cttaaaatat	aaacttggtt	cacaagcttt	aatccatgtg	180
gatttttttt	cttagagaac	cacaaaacat	aaaaggagca	agtcggactg	aatacctgtt	240
tccatagtgc	ccacagggta	ttcctcacat	tttctccata	ggaaaatgct	ttttcccaag	300
g						301

<210> 254

<211> 301

<212> DNA

<213> Homo sapien

<400> 254

cgctgcgcct	ttcccttggg	ggaggggcaa	ggccagaggg	ggtccaagtg	cagcacgagg	60
aacttgacca	attcccttga	agcgggtggg	ttaaaccctg	taaattggaa	caaaatcccc	120
ccaaatctct	tcattcttacc	ctgggtggact	cctgactgta	gaattttttg	gttgaaacaa	180
gaaaaaaata	aagcttttga	cttttcaagg	ttgcttaaca	ggtactgaaa	gactggcctc	240
acttaactg	agccaggaaa	agctgcagat	ttattaatgg	gtgtgttagt	gtgcagtgcc	300
t						301

<210> 255

<211> 302

<212> DNA

<213> Homo sapien

<400> 255

agcttttttt	tttttttttt	tttttttttt	ttcattaaaa	aatagtgtc	tttattataa	60
attactgaaa	tgtttctttt	ctgaatataa	atataaatat	gtgcaaagt	tgacttggat	120
tgggattttg	ttgagttctt	caagcatctc	ctaataccct	caagggcctg	agtagggggg	180
aggaaaaagg	actggaggtg	gaatctttat	aaaaaacaag	agtgattgag	gcagattgta	240
aacattatta	aaaaacaaga	aacaaacaaa	aaaatagaga	aaaaaacac	cccaacacac	300
aa						302

<210> 256

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 256

gttccagaaa	acattgaagg	tggtctccca	aagtctaact	agggataccc	cctctagcct	60
aggaccctcc	tccccacacc	tcaatccacc	aaaccatcca	taatgcaccc	agataggccc	120
acccccaaaa	gcctggacac	cttgagcaca	cagttatgac	caggacagac	tcattcttat	180
aggcaaatag	ctgctggcaa	actggcatta	cctggtttgt	ggggatgggg	gggcaagtgt	240
gtggcctctc	ggcctgggta	gcaagaacat	tcagggtagg	cctaagttan	tcgtgttagt	300
t						301

<210> 257

<211> 301

<212> DNA

<213> Homo sapien

86

<400> 257
 gttgtggagg aactctgggt tgctcattaa gtcctactga ttttactat cccctgaatt 60
 tccccactta tttttgtott tcactatcgc aggccttaga agaggtctac ctgcctccag 120
 tcttacctag tccagtctac ccctggagt tagaatggcc atcctgaagt gaaaagtaat 180
 gtcacattac tcccttcagt gatttcttgt agaagtgcc atccctgaat gccaccaaga 240
 tcttaatctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc 300
 c 301

<210> 258
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 258
 cagcagtagt agatgccgta tgccagcagc ccagcactc ccaggatcag caccagcacc 60
 aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120
 cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg 180
 atgtctcggg cattgaggct gtcaataana cgctgatccc ctgtgtatg gtggtgtcat 240
 tgggtgatccc tgggagcgcc ggtggagtaa cgttgggtcca tggaaagcag cgcccacaac 300
 t 301

<210> 259
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 259
 tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg 60
 gtgtcctgaa gtgatttggg ccctgaggg cagacacctg agtaggaatc ccagtgggaa 120
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggcccag gaaggtctgt 180
 tccagctcac atctcatctg catgcagcac ggaccggatg cgcccaactg gtcttggctt 240
 ccctccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccagggtg 300
 c 301

<210> 260
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 260
 ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatggt 60
 aaggtgtctt aacttgaaaa agattaggag tcaactgggtt acaagttata attgaatgaa 120
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacia caggattaac 180
 tagggcaaaa taaataagtg tgtggaagcc ctgataagtg ctttaataaac agactgattc 240
 actgagacat cagtacctgc ccgggcggcc gtcgagccg aattctgcag atatccatca 300
 c 301

<210> 261
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 261
 aaatattcga gcaaattcctg taactaatgt gtctccataa aaggctttga actcagtga 60
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggtt 120
 agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggttcaat 180
 ggtgacatcc aattttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240
 ggcattgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300
 a 301

<210> 262
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 262
 gaggagagcc tggtacagca ttgtgaagca cagaatactc caggagtatt tgtaattgtc 60
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaattc ctgagtcacc 120
 cctagacttc ctaaaccaga tctctcgggg ctggaacctg gcactctgca ttgtaatga 180
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgtcc 240
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300
 c 301

<210> 263
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 263
 tttagcttgt ggtaaattgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60
 aaaattacta cttaattccta attcacaata acaatggcat taagggttga ctgagtttg 120
 ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat 180
 taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg 240
 agatgctaag gcccagaga togtttgatc caacctctt attttcagag gggaaaatgg 300
 g 301

<210> 264
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 264
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60
 aatgaatgac tctaaaaaca atatttacat ttaatgggtt gtagacaata aaaaaacaag 120
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
 acccttcata taaattcact atcttggtt gaggcactcc ataaaatgta tcacgtgcat 300
 a 301

<210> 265

<211> 301
 <212> DNA
 <213> Homo sapien

<400> 265
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt 60
 cttcttgtga cgcagtatct cttctctggg gagaagccgg gaagtcttct cctggctcta 120
 catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga 180
 ttttcagttt gtcaacatgt tctctaaca cacttgccca tttctgtaaa gaatccaaag 240
 cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300
 c 301

<210> 266
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 266
 taccgtctgc ctttctctcc atccaggcca tctgcgaatc tacatgggtc ctctatttgc 60
 acaccagatc actcttttct ctaccacag gcttgctatg agcaagagac acaacctctc 120
 ctcttctgtg ttccagcttc ttttctgtt cttccacccc ctttaagttct attcctgggg 180
 atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca ggggtgcacag 240
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgctg 300
 a 301

<210> 267
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 267
 aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg 60
 gttctcagtg ctgagtcctc ccaggaaaag ctcacctaga cttcttgagg ctgaatcttc 120
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaagc 180
 ctcatctga ttctctctct tcttttcttt caagttggct ttctcacat ccctctgttc 240
 aattcgcttc agcttgtctg ctttagccct catttcacaga agcttcttct ctttggcctc 300
 t 301

<210> 268
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 268
 aatgtctcac tcaactactt ccagcctac cgtggcctaa ttctgggagt tttcttctta 60
 gatcttggga gagctgggtc ttctaaggag aaggaggaag gacagatgta actttggatc 120
 tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttgggaata 180
 tgctgggttg ctcagtgagc ctttttgag aaagcaagta ttattcttaa ggagtaacca 240
 cttccatttg ttctacttct taccatcatc aattgtatat tatgtattct ttggagaact 300
 a 301

<210> 269
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 269
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60

89

```

aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact 120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta 180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta 240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc 300
t 301

```

```

<210> 270
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120
gagcttgctg gtgcagtgc tttggataa cactattcat ggccgaattg atcaagtcaa 180
ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240
tggaaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300
a 301

```

```

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 271
aaaaggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60
tttatagctc atcttttaggg ttgatattca gttcatgctt cccttgctgt tottgatcca 120
gaattgcaat cacttcatca gcctgtattc gctcgaattc tctataaagt ggggtccaagg 180
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
tctctcctcc agatganaac tgatcatgcy cccacatttt ggggtttata gaagcagtca 300
c 301

```

```

<210> 272
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180
gcattctctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240
ctaaggactt ccattgcatc tctacaata ttttctctac gcaccactag aattaagcag 300
g 301

```

```

<210> 273
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)

```


acatgtgtgt	atgtgtatct	ttgggaaaaan	aanaagacat	cttgtttayt	attttttttg	60
agagangctg	ggacatggat	aatcacwtaa	tttgctayta	tyactttaat	ctgactygaa	120
gaaccgtcta	aaaataaaaat	ttaccatgtc	dtatatccct	tatagtatgc	ttatttcacc	180
ttytttctgt	ccagagagag	tatcagtgac	ananatttma	gggtgaamac	atgmattggt	240
gggacttnty	tttacngagm	accctgcccg	sgcgcctcg	makcngantt	ccgcsananc	300
t						301

<213> Homo sapien

<223> n = A, T, C or G

cttatatact	ctttctcaga	ggcaaaagag	gagatgggta	atgtagacaa	ttctttgagg	60
aacagtaa	gattattaga	gagaangaat	ggaccaagga	gacagaaatt	aacttgtaaa	120
tgattctctt	tggaatctga	atgagatcaa	gaggccagct	ttagcttg	gaaaagtcca	180
tctaggtatg	gttgcatctt	cgtcttcttt	tctgcagtag	ataatgaggt	aaccgaaggc	240
aattgtgctt	cttttgataa	gaagctttct	tggtcata	tc	aggaaattcc	300
c					aganaaagtc	301

<213> Homo sapien

<223> n = A, T, C or G

tcggtgtcag	cagcacgtgg	cattgaacat	tgcaatgtgg	agcccaaacc	acagaaaatg	60
gggtgaaatt	ggccaacttt	ctattaactt	atgttggtcaa	ttttgccacc	aacagtaagc	120
tggcccttct	aataaaaaga	aattgaaagg	tttctcacta	aacggaatta	agtagtgagg	180
tcaagagact	cccaggcctc	agcgtacctg	cccggggcggc	cgctcgaagc	cgaattctgc	240
agatatccat	cacactggcg	gncgctcgan	catgcatcta	gaaggnccaa	ttcgccctat	300
a						301

<213> Homo sapien

tgtagacata	ctcaataaat	aaatgactgc	atttgtggtat	tattactata	ctgattatat	60
ttatcatgtg	acttctaatt	agaaaatgta	tccaaaagca	aaacagcaga	tatacaaaat	120
taaagagaca	gaagatagac	attaacagat	aaggcaactt	atacattgag	aatccaaatc	180
caatacattt	aaacatttgg	gaaatgaggg	ggacaaatgg	aagccagatc	aaatttgtgt	240
aaaactattc	agtatgtttc	ccttgcttca	tgtctgagaa	ggctctcctt	caatggggat	300
g						301

<210> 277
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 277
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaagaag gaaaacattg 120
 gaatcatggc actoctgata ctttcccaaa tcaacactct caatgcccc ccctcgtcct 180
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240
 gttcnctgtc gattacatct gaccagtctc ctttttccga agtccttccg ttcaatcttg 300
 c 301

<210> 278
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 278
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacaggttt 240
 tatgtgttct tcgttaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300
 c 301

<210> 279
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 279
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120
 ttagaccttt acctccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300
 a 301

<210> 280
 <211> 301
 <212> DNA

<213> Homo sapien

<400> 280

ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg	60
tagaaagggtg gtggaaccaa attgtgggtca atggaaatag gagaatatgg ttctcactct	120
tgagaaaaaa acctaaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg	180
gtttgatata gtttaggggtt ggggttagat taagatctaa attacatcag gacaaagaga	240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag	300
t	301

<210> 281

<211> 301

<212> DNA

<213> Homo sapien

<400> 281

aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc	60
gccgagcaat ccaaatoctg aatgaagggg catcttctga aaaaggagat ctgaatctca	120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa	180
tgtgtagcac actgcgatta cagctaaata acccgatttt gtgtgtcatg ttgcatcttc	240
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc	300
g	301

<210> 282

<211> 301

<212> DNA

<213> Homo sapien

<400> 282

caggtaactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca	60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga	120
agcgagaag caaagcccag gcagaacccat gctaacctta cagctcagcc tgcacagaag	180
cgagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg	240
cagaagcaaa gcccaggcag aacatgctaa cttacagct cagcctgcac agaagcacag	300
a	301

<210> 283

<211> 301

<212> DNA

<213> Homo sapien

<400> 283

atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag	60
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca	120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc	180
acttcccagg ttttatgcaa aaattttggt aaattctata atggtgatat gcatctttta	240
ggaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt	300
g	301

<210> 284

<211> 301

<212> DNA

<213> Homo sapien

<400> 284

caggtaacaaa acgctattaa gtggcttaga attgaacat ttgtggtctt tatttacttt	60
gcttcgtgtg ttggcaaagc aacatcttcc ctaaataat attaccaaga aaagcaagaa	120
gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat	180

ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240
 actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt 300
 a 301

<210> 285

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 285

acatcacat gatcgatcc cccacccatt atacgttgta tgtttacata aatactcttc 60
 aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
 caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
 attaaatatg tctgacttct tttgaggta cagcatagg caaatgctat ttacgatctg 240
 caaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300
 t 301

<210> 286

<211> 301

<212> DNA

<213> Homo sapien

<400> 286

taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60
 tgtatattat ttttgcccta cagtggatca ttctagtagg aaaggacagt aagatttttt 120
 atcaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180
 aaaataagct accatatagc ttataagtct caaatttttg cttttacta aaatgtgatt 240
 gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg 300
 t 301

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<400> 287

tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60
 ccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg 120
 aaatgatttg gttatgaacg cacagttag gcagcagggc cagaatcctg accctctgcc 180
 ccgtggttat ctctcccca gcttggctgc ctcatgttat cacagtattc cattttgttt 240
 gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggaatgc 300
 t 301

<210> 288

<211> 301

<212> DNA

<213> Homo sapien

<400> 288

gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
 agtcaatagg aagacaaatt ccagttccag ctcatcttgg gtatctgcaa agctgcaaaa 120
 gatcttttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatc 180
 aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag 240

tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300
a 301

<210> 289
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 289
ggtacactgt ttccatgta tgtttctaca cattgctacc tcagtgtcc tggaaactta 60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggg ggccggcgaan aagagaaaga 240
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga 300
a 301

<210> 290
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 290
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60
tgactgatct gttcatttct ctcacagctc ttacccccaa aagcttttcc accctaagtg 120
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc 240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtga 300
a 301

<210> 291
<211> 301
<212> DNA
<213> Homo sapien

<400> 291
caggtagcaa tttcttctat cctagaaaca tttcatttta tgttggtgaa acataacaac 60
tatatcagct agattttttt tctatgcttt acctgotatg gaaaatttga cacattctgc 120
ttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa 240
acatgagctt cacttcccca ctaactaatt agcatctggt atttcttaac cgtaatgcct 300
a 301

<210> 292
<211> 301
<212> DNA
<213> Homo sapien

<220>

95

<221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 292
 accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc 60
 tgtattaaat aattttttaag tttaaaagat aaaataccat catttttaaat gttggtattc 120
 aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaaatgat ttgcnagatg 180
 ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc 240
 tcactacaca cacagacccc acagtccctat atgccacaaa cacatttcca taacttgaaa 300
 a 301

<210> 293
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 293
 ggtaccaagt gctgggtgcc gcctgttacc tgttctcact gaaaagtctg gctaattgctc 60
 ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactggt 120
 aacacaaaag tcaactagcaa agtagcaaca gcttttaagtc taaatacaaa gctgtttctgt 180
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcattttttaa tgtacctcgg 240
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcgggc gctcgagcat 300
 g 301

<210> 294
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 294
 tgacccataa caatatacac tagctatctt ttttaactgtc catcattagc accaatgaag 60
 attcaataaa attaccttta ttcaacacatc tcaaaaacaat totgcaaatt cttagtgaag 120
 ttttaactata gtcacaganc ttaaattatc acattgtttt ctatgtctac tgaaaataag 180
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240
 cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt 300
 t 301

<210> 295
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 295
 gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta 60
 cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttgtg aatccatctt gctttttccc catttggaact agtcattaac ccatctctga 180
 actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggatga attggatggg 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300
 tctct 305

<210> 296
 <211> 301

```
<212> DNA
<213> Homo sapien
```

```

<400> 296
agggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct    60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg    120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac    180
tttgaaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt    240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg    300
c                                                    301

```

```
<210> 297
<211> 300
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(300)
<223> n = A,T,C or G
```

<400> 297						
actgagtttt	aactggacgc	caagcaggca	aggctggaag	gttttgctct	ctttgtgcta	60
aaggtttttga	aaaccttgaa	ggagaatcat	tttgacaaga	agtacttaag	agtctagaga	120
acaaacangt	gaaccagctg	aaagctctcg	ggggaanctt	acatgtgttg	ttaggcctgt	180
tcocatcttg	ggagtcgact	ggccatccct	caaaatttgc	ctgggctggc	ctgagtggtc	240
accgcacctc	ggccgcgacc	acgctaagcc	gaattctgtc	gatatccatc	acactggcgg	300

```
<210> 298
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
```

<400> 298							
tatgggggttt	gtcacccaaa	agctgatgct	gagaaaggcc	tccctggggc	ccctccgcgc		60
ggcatctgag	agacctggtg	ttccagtggt	tctggaaatg	ggtccagtg	ccgcgggctg		120
tgaagctctc	agatcaatca	cgggaagggc	ctggcgggtg	tggccacctg	gaaccaccct		180
gtcctgtctg	tttacatttc	actaycaggt	tttctctggg	cattacnatt	tgttccccta		240
caacagtgac	ctgtgcattc	tgctgtggcc	tgctgtgtct	gcaggtggct	ctcagcgagg		300
t							301

```
<210> 299
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 299

gttttgagac	ggagtttcac	tcttgttgcc	cagactggac	tgcaatggca	gggtctctgc	60
tcactgcacc	ctctgcctcc	caggttcgag	caattctcct	gcctcagcct	cccaggtagc	120
tgggattgca	ggctcacgcc	accataccca	gctaattttt	ttgtattttt	agtagagacg	180
gagtttcgcc	atgttggcca	gctggtotca	aactcctgac	ctcaagcgac	ctgcctgcct	240
cggcctccca	aagtgctgga	attataggca	tgagtcaaca	cgcccagcct	aaagatatatt	300
t						301

<210> 300
<211> 301
<212> DNA
<213> Homo sapien

<400> 300
attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tottgccaga 60
tatgtcccac acccactggg aaaggctccc acctggctac ttctctctatc agctgggtca 120
gctgcattcc acaaggttct cagcctaattg agtttacta cctgccagtc tcaaaactta 180
gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggttac 240
tataaagcct gcctctaaca gtccttgctt ottcacacca atcccgagcg catcccccat 300
g 301

<210> 301
<211> 301
<212> DNA
<213> Homo sapien

<400> 301
ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120
gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaaagacc 180
ctcagagctg agacacccac aacagtggga gtcacaaaag accctcagag ctgagacacc 240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300
t 301

<210> 302
<211> 301
<212> DNA
<213> Homo sapien

<400> 302
aggtacacat ttagcttggtg gtaaatgact cacaaaactg attttaaaaat caagttaatg 60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240
caggatttga gatgctaagg cccagagat cgtttgatcc aaccctctta ttttcagagg 300
g 301

<210> 303
<211> 301
<212> DNA
<213> Homo sapien

<400> 303
aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt 60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120
tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc 180
agtaacgggt atgtttttct aactgatott ttgctcgttc caaagggacc tcaagacttc 240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300
c 301

<210> 304
<211> 301
<212> DNA
<213> Homo sapien

<400> 304

acatggatgt	tattttgcag	actgtcaacc	tgaatttgta	tttgcttgac	attgcctaatt	60
tattagtttc	agtttcagct	tacccacttt	ttgtctgcaa	catgcaraas	agacagtgcc	120
cttttttagtg	tatcataatca	ggaatcatct	cacattgggt	tgtgccatta	ctgggtgcagt	180
gacttttcagc	cacttgggta	aggtggagtt	ggccatatgt	ctccactgca	aaattactga	240
ttttcctttt	gtaattaata	agtgtgtgtg	tgaagaattct	ttgagatgag	gtatataatct	300
c						301

<210> 305

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 305

gangtacagc	gtggtcaagg	taacaagaag	aaaaaatgt	gagtggcatc	ctgggatgag	60
cagggggaca	gacctggaca	gacacgttgt	catttgctgc	tgtgggtagg	aaaatgggag	120
taaaggagga	gaaacagata	caaatctcc	aactcagtat	taaggatttc	tcatgcctag	180
aatattggta	gaaacaagaa	tacattcata	tggcaataaa	ctaaccatgg	tggaaacaaa	240
ttctgggatt	taagttggat	accaangaaa	ttgtattaaa	agagctgttc	atggaataag	300
a						301

<210> 306

<211> 8

<212> PRT

<213> Homo sapien

<400> 306

Val	Leu	Gly	Trp	Val	Ala	Glu	Leu
1				5			

<210> 307

<211> 637

<212> DNA

<213> Homo sapien

<400> 307

acagggatg	aagggaagg	gagaggatga	ggaagccccc	ctggggattt	ggtttggtcc	60
ttgtgatcag	gtggtctatg	gggcttatcc	ctacaaagaa	gaatccagaa	ataggggcac	120
attgaggaat	gatacttgag	cccaaagagc	attcaatcat	tgttttattt	gccttmtttt	180
cacaccattg	gtgagggagg	gattaccacc	ctgggggttat	gaagatgggt	gaacacccca	240
cacatagcac	cggagatatg	agatcaacag	tttcttagcc	atagagattc	acagcccaga	300
gcaggaggac	gcttgcacac	catgcaggat	gacatggggg	atgcgctcgg	gattggtgtg	360
aagaagcaag	gactgttaga	ggcaggcttt	atagtaacaa	gacggtgggg	caaactctga	420
tttcggtggg	ggaatgtcat	ggtcttgctt	tactaagttt	tgagactggc	aggtagtga	480
actcattagg	ctgagaacct	tgtggaatgc	acttgaccca	sctgatatag	gaagtagcca	540
ggtgggagcc	tttcccagtg	ggtgtgggac	atatctggca	agattttgtg	gcactcctgg	600
ttacagatac	tggggcagca	aataaaactg	aatcttg			637

<210> 308

<211> 647

<212> DNA

<213> Homo sapien

99

<220>
 <221> misc_feature
 <222> (1)...(647)
 <223> n = A,T,C or G

<400> 308
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60
 tgctcagggg aaggttcata tgggactttc tactgcccaa gggtctatac aggatataaa 120
 ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180
 ccaccctctt gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg 240
 ctagagaaaa gaccaacaac ggccctcaaag gatctcttac catgaaggtc tcagctaatt 300
 cttgggctaag atgtgggttc cacattaggt tctgaatatg gggggaagg tcaatttgct 360
 cattttgtgt gtggataaaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 420
 gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480
 tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 540
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309
 <211> 460
 <212> DNA
 <213> Homo sapien

<400> 309
 actttatagt ttaggctgga cattggaaaa aaaaaaaagc cagaacaaca tgtgatagat 60
 aatatgattg gctgcacact tocagactga tgaatgatga acgtgatgga ctattgtatg 120
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180
 accaaacatc atgccagaat actcagcaaa ccttcttagc tottgagaag tcaaagtcag 240
 ggggaattta ttcttgcaa ttttaattgg actccttatg tgagagcagc ggctaccag 300
 ctgggggtgt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc 360
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 420
 ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310
 <211> 539
 <212> DNA
 <213> Homo sapien

<400> 310
 acgggactta tcaataaaag ataggaaaag aagaaaactc aaatattata ggcagaaatg 60
 ctaaagggtt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 120
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180
 gtcagacagt aagatttgtg ggaaatgggt tgggtttgtg tatgggtatg attttagcaa 240
 taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa 300
 ttcttcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac 360
 ctatagatgaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac 420
 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc 480
 atattttcac cccacaaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 539

<210> 311
 <211> 526
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(526)
 <223> n = A,T,C or G

100

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<400> 311
caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc      60
ttttgacgtt ttotctaaac tactaaagag gcattaatga tccataaatt atattatcta      120
catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa      180
attaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg      240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa      300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc      360
tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc      420
acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa      480
agttctataa actgtagtnt acttatttta atcccaaaag cacagt                    526

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<210> 312
<211> 500
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(500)
<223> n = A,T,C or G

```

```

<400> 312
cctctctctc cccaccccct gactctagag aactggggtt tctcccagta ctccagcaat      60
tcattttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct      120
ccattttctct ttoccttcca cctgccagtt ttgctgactc tcaacttgtc atgagtgtaa      180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg      240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atcccctctt      300
tgcagatgtc tagcagcttc agacatttgg ttaagaacct atgggaaaaa aaaaaatcct      360
tgctaattgt gtttcctttg taaaccanga ttcttatttg nctgggtatag aatatcagct      420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt      480
tagtcttaat tatctattgg                    500

```

```

<210> 313
<211> 718
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(718)
<223> n = A,T,C or G

```

```

<400> 313
ggagatttgt gtggtttgca gccgagggag accaggaaga tctgcatggt gggaaggacc      60
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat      120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa      180
gtagtacat gtttttgcac atttcagcc cttttaaata tccacacaca caggaagcac      240
aaaaggaagc acagagatcc ctgggagaaa tgcccgcccg ccatottggg tcatcgatga      300
gcctcgccct gtgcctgntc ccgcttgatg gggaaggaca ttagaaaatg aattgatgtg      360
ttccttaaag gatggcagga aaacagatcc tgttgatgat atttatttga acgggattac      420
agatttgaaa tgaagtcaca aagtgcagat taccaatgag aggaaaaacag acgagaaaat      480
cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc      540
aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg      600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaataac tgacttacgg      660
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<210> 314

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<211> 358
 <212> DNA
 <213> Homo sapien

<400> 314
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 gctctcggtg gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc 240
 ttgttgtatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttget 300
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<210> 315
 <211> 341
 <212> DNA
 <213> Homo sapien

<400> 315
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 gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag cccaatgac 180
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<210> 316
 <211> 151
 <212> DNA
 <213> Homo sapien

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 <212> DNA
 <213> Homo sapien

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 ccagggtctt gttcttgcca cacctgcttg a 151

<210> 318
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 318
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<210> 319
 <211> 151
 <212> DNA

102

<213> Homo sapien

<400> 319

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catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg	120
taagattggg tttatgtgat tttagtgggt a	151

<210> 320

<211> 150

<212> DNA

<213> Homo sapien

<400> 320

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gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt	120
gagtgttcta cagcttacag taaataccat	150

<210> 321

<211> 151

<212> DNA

<213> Homo sapien

<400> 321

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<210> 322

<211> 151

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (151)

<223> n = A,T,C or G

<400> 322

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<210> 323

<211> 151

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (151)

<223> n = A,T,C or G

<400> 323

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gttcaatyaa aaagacatt ancccatgtg g	151

<210> 324

103

<211> 461
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(461)
 <223> n = A,T,C or G

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 cacacaaatg caatagtttg tcaactgcat ttacactgaa ccaaagctaa acccggtgtt 360
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 aaaaacgcac aagagccctt gccctgccct agctgangca c 461

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 <211> 400
 <212> DNA
 <213> Homo sapien

<400> 325
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<210> 326
 <211> 1215
 <212> DNA
 <213> Homo sapien

<400> 326
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104

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 aaaaaaaaaa aaaaa 1215

<210> 327
 <211> 220
 <212> PRT
 <213> Homo sapien

<400> 327
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 20 25 30
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
 35 40 45
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
 50 55 60
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
 65 70 75 80
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
 180 185 190
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
 195 200 205
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 328
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 atccgcagtg ggtgctgtca gccacacact gtttcagaaa ctctacacc atcgggctgg 180
 gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag gcca 234

<210> 329
 <211> 77
 <212> PRT
 <213> Homo sapien

<400> 329
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 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu

105

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Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Ser	Ala	Thr
		35					40					45			
His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu
	50					55					60				
Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val	Glu	Ala			
65					70					75					

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<210> 330
<211> 70
<212> DNA
<213> Homo sapien
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<400> 330
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gctgcagcca 70

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<210> 331
<211> 22
<212> PRT
<213> Homo sapien
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<400> 331
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Val Ser Gly Ser Cys Ser
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<210> 332
<211> 2507
<212> DNA
<213> Homo sapien
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<400> 332						
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 <211> 3030
 <212> DNA
 <213> Homo sapien

<400> 333						
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<210> 334

<211> 2417

<212> DNA

<213> Homo sapien

<400> 334

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<211> 2984

<212> DNA

<213> Homo sapien

<400> 335

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109

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<210> 336
<211> 147
<212> PRT
<213> Homo sapien

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<400> 336
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Leu Asp Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr
20          25          30
Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
35          40          45
Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
50          55          60
Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
65          70          75          80
Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
85          90          95
Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
100          105          110
Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
115          120          125
Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
130          135          140
Ala Phe Trp
145

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<210> 337
<211> 9
<212> PRT
<213> Homo sapien

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<400> 337
Ala Leu Thr Gly Phe Thr Phe Ser Ala
1          5

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<210> 338
<211> 9
<212> PRT
<213> Homo sapien

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<400> 338
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1          5

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<210> 339
<211> 318
<212> PRT
<213> Homo sapien

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110

<400> 339
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 20 25 30
 Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly
 35 40 45
 Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg
 50 55 60
 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu
 65 70 75 80
 Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val
 85 90 95
 Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys
 100 105 110
 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala
 115 120 125
 Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met
 130 135 140
 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu
 145 150 155 160
 Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser
 165 170 175
 Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly
 180 185 190
 Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala
 195 200 205
 Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly
 210 215 220
 Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val
 225 230 235 240
 Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe
 245 250 255
 Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu
 260 265 270
 Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His
 275 280 285
 Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg
 290 295 300
 Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp
 305 310 315

<210> 340
 <211> 483
 <212> DNA
 <213> Homo sapien

<400> 340
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 ctg 483

111

<210> 341
 <211> 344
 <212> DNA
 <213> Homo sapien

<400> 341
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 gctgccttac aagtattataa tatttttactt ctttocataa agagtagctc aaaatatgca 180
 attaatttaa taattttctga tgatgggttt atctgcagta atatgtatat catctattag 240
 aattttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc 300
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<210> 342
 <211> 592
 <212> DNA
 <213> Homo sapien

<400> 342
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 cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg 180
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 agttcttctt ggtttgtgat gtcttttctg ctttccatta attctataaa atagtatggc 540
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<210> 343
 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 343
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 aaaccaccaa gctgaaaaaa aa 382

<210> 344
 <211> 536
 <212> DNA
 <213> Homo sapien

<400> 344
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112

caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctagccctaa 480
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<210> 345
<211> 251
<212> DNA
<213> Homo sapien

<400> 345
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gcgtgggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga 180
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gtgccatttc c 251

<210> 346
<211> 282
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(282)
<223> n = A,T,C or G

<400> 346
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agaaaggctt tctatttcac tggcccagggt agggggaagg agagtaactt tgagtctgtg 240
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<210> 347
<211> 201
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(201)
<223> n = A,T,C or G

<400> 347
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tctgagactg actggaccca cccagaccca gggcaaagat acatgttacc atatcatctt 180
tataaagaat ttttttttgt c 201

<210> 348
<211> 251
<212> DNA
<213> Homo sapien

<400> 348
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aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg 180
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gccctgcctc c 251

<210> 349

<211> 251

<212> DNA

<213> Homo sapien

<400> 349

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<210> 350

<211> 908

<212> DNA

<213> Homo sapien

<400> 350

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<210> 351

<211> 472

<212> DNA

<213> Homo sapien

<400> 351

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tcagccccct tttggcctgt ttgttttgtc aaaaacctaa tctgcttctt gcttttcttg	420
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<210> 352

<211> 251

<212> DNA

<213> Homo sapien

<400> 352

114

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caggctgcgt	tccgtcctta	cgatgaagac	cacgatgcag	tttccaaaca	ttgccactac	180
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aataagcaca	a					251

<210> 353
 <211> 436
 <212> DNA
 <213> Homo sapien

<400> 353						
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gtatccaaaa	gcaaacacgc	agatatacaa	aattaaagag	acagaagata	gacattaaca	180
gataaggcaa	cttatacatt	gacaatccaa	atccaataca	tttaaacatt	tgggaaatga	240
gggggacaaa	tgggaagccar	atcaaatttg	tgtaaaacta	ttcagtatgt	ttcccttgct	300
tcatgtctga	raaggctctc	ccttcaatgg	ggatgacaaa	ctccaaatgc	cacacaaatg	360
ttaacagaat	actagattca	cactggaacg	ggggtaaaga	agaaattatt	ttctataaaa	420
gggtccttaa	tgtagt					436

<210> 354
 <211> 854
 <212> DNA
 <213> Homo sapien

<400> 354						
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caagtctgaa	accaaatacta	gaaacatag	gaaacgagcc	aggcacaggg	ctgggtgggcc	120
atcagggacc	accctttggg	ttgatatttt	gcttaatctg	catcttttga	gtaagatcat	180
ctggcagtag	aagctgttct	ccagggtacat	ttctctagct	catgtacaaa	aacatcctga	240
aggactttgt	cagggtgcctt	gctaaaagcc	agatgcgttc	ggcacttcct	tggtctgagg	300
ttaattgcac	acctacaggc	actgggctca	tgctttcaag	tattttgtcc	tacttttagg	360
gtgagtgaag	gatccccatt	ataggagcac	ttgggagaga	tcatataaaa	gctgactcct	420
gagtacatgc	agtaaatggg	tagatgtgtg	tggtgtgtct	tcattoctgc	aagggtgctt	480
gttagggagt	gtttccagga	ggaacaagtc	tgaaaccaat	catgaaataa	atggtaggtg	540
tgaactggaa	aactaattca	aaagagagat	cgtgatatca	gtgtggttga	tacaccttgg	600
caatatggaa	ggctctaatt	tgccatatt	tgaataata	attcagcttt	ttgtaataca	660
aaataacaaa	ggattgagaa	tcatggtgtc	taatgtataa	aagacccagg	aaacataaat	720
atatcaactg	cataaatgta	aaatgcatgt	gaccaagaa	ggcccaaaag	tggcagacaa	780
cattgtaccc	attttccctt	ccaaaatgtg	agcggcgggc	ctgctgcttt	caaggctgtc	840
acacgggatg	tcag					854

<210> 355
 <211> 676
 <212> DNA
 <213> Homo sapien

<400> 355						
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atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
gacagcatcg	ctgtaaaaag	cctaccaatg	agagctcagt	tcaaggcgaa	ccacccttc	240
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ccctaatacag	atgggggttga	gtaaggctca	gagttgcaga	tgaggtgcag	agacaatcct	360
gtgactttcc	cacggccaaa	aagctgttca	cacctcacgc	acctctgtgc	ctcagtttgc	420
tcatctgcaa	aataaggtcta	ggatttcttc	caaccatttc	atgagttgtg	aagctaaggc	480
tttggttaatc	atggaaaaag	gtagacttat	gcagaaagcc	tttctggctt	tcttatctgt	540

115

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ggtgtctcat ttgagtgtc tccagtgtc tgatcaagtc aatgagtaaa attttaaggg 600
attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgtacc tgacatctct 660
gcttaaagaa aaccag 676

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<210> 356
<211> 574
<212> DNA
<213> Homo sapien

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<400> 356
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catgtggcac ctgactggca tcaaaccaaa gttcgttaggc caacaaagat gggccactca 120
caagcttccc atttgtagat ctcagtgcct atgagtatct gacacctgtt cctctcttca 180
gtctcttagg gaggttataa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc 240
aaaagtccac aaaactgcag tctttgtctg gatagtaagc caagcagtgc ctggacagca 300
gagttctttt cttgggcaac agataaccag acaggactct aatcgtgtct ttattcaaca 360
ttcttctgtc tctgcctaga ctggaataaa aagccaatct ctctcgtggc acaggaagg 420
agatacaagc tcgtttacat gtgatagatc taacaaaggc atctaccgaa gtctggtctg 480
gatagacggc acagggagct cttaggctcag cgctgctggt tggaggacat tctgagtcc 540
agcttttgag cctttgtgca acagtacttt ccca 574

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<210> 357
<211> 393
<212> DNA
<213> Homo sapien

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<400> 357
tttttttttt tttttttttt tttttttttt tacagaatat aratgcttta tcaactgkact 60
taatatggkg kcttyttcac tatacttaaa aatgcaccac tcataaatat ttaattcagc 120
aagccacaac caaracttga ttttatcaac aaaaaccctt aaatataaac ggsaaaaaag 180
atagatatata ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara 240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa 300
gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct 360
tttttttctt tttctgtttt tttttttttt tac 393

```

```

<210> 358
<211> 630
<212> DNA
<213> Homo sapien

```

```

<400> 358
acagggtaaa caggaggatc cttgctctca cggagcttac attctagcag gaggacaata 60
ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga 120
gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg 180
gagtttaaac tgagagaagc aagtgcctaa actgaaggat gtgttgaaaga agaagggaga 240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaaagaact 300
gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag 360
attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa 420
tcaactgaag gagtaatgtg acattacttt tcaactcagg atggccattc taactccagg 480
gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcatagat 540
gaaagacaaa aataagtggg gaaattcagg ggatagttaa aatcagtagg acttaatgag 600
caagccagag gttcctccac aacaaccagt 630

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<210> 359
<211> 620
<212> DNA
<213> Homo sapien

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116

<400> 359

acagcattcc	aaaatataca	tctagagact	aarrgtaaat	gctctatagt	gaagaagtaa	60
taattaaaa	atgctactaa	tatagaaaat	ttataatcag	aaaaataaat	attcagggag	120
ctcaccagaa	gaataaagt	ctctgccagt	tattaaagga	ttactgctgg	tgaattaaat	180
atggcattcc	ccaagggaaa	tagagagatt	cttctggatt	atgttcaata	tttatttcac	240
aggattaact	gttttaggaa	cagatataaa	gcttcgccac	ggaagagatg	gacaaagcac	300
aaagacaaca	tgatacctta	ggaagcaaca	ctacccttcc	aggcataaaa	tttgagaaaa	360
tgcaacatta	tgcttcatga	ataatatgta	gaaagaaggt	ctgatgaaaa	tgacatcctt	420
aatgtaagat	aactttataa	gaattctggg	tcaaataaaa	ttctttgaag	aaaacatcca	480
aatgtcattg	acttatcaaa	tactatcttg	gcatataacc	tatgaaggca	aaactaaaca	540
aacaaaaagc	tcacacccaa	caaaaccatc	aacttatttt	gtattctata	acatacgaga	600
ctgtaaagat	gtgacagtgt					620

<210> 360

<211> 431

<212> DNA

<213> Homo sapien

<400> 360

aaaaaaaaaa	agccagaaca	acatgtgata	gataatatga	ttggctgcac	acttcagac	60
tgatgaatga	tgaacgtgat	ggactattgt	atggagcaca	tcttcagcaa	gagggggaaa	120
tactcatcat	ttttggccag	cagttgtttg	atcaccaaac	atcatgccag	aatactcagc	180
aaaccttctt	agctcttgag	aagtcaaagt	ccgggggaat	ttattcctgg	caattttaat	240
tggaactcctt	atgtgagagc	agcggctacc	cagctggggt	ggtggagcga	acccgtcact	300
agtggaacatg	cagtggcaga	gtccttggtg	accacctaga	ggaatacaca	ggcacatgtg	360
tgatgccaag	cgtgacacct	gtagcactca	aatttgtctt	gtttttgtct	ttcgggtgtgt	420
agattcttag	t					431

<210> 361

<211> 351

<212> DNA

<213> Homo sapien

<400> 361

acactgattt	ccgatcaaaa	gaatcatcat	ctttaccttg	acttttcagg	gaattactga	60
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ttgggtcctc	tggtctcttg	ccaagtctcc	cagccactcg	agggagaaat	atcgggaggt	180
ttgacttcct	ccggggcttt	cccaggggct	tcaccgtgag	ccctgcggcc	ctcagggctg	240
caatcctgga	ttcaatgtct	gaaacctcgc	tctctgcctg	ctggacttct	gaggccgtca	300
ctgccactct	gtcctccagc	tctgacagct	cctcatctgt	ggtcctgttg	t	351

<210> 362

<211> 463

<212> DNA

<213> Homo sapien

<400> 362

acttcatcag	gccataatgg	gtgcctcccg	tgagaatcca	agcacctttg	gactgcgcga	60
tgtagatgag	ccggtgaag	atcttgccga	tgccgggctt	cagggcgaag	ttcttggcgc	120
ccccggtcac	agaaatgacc	aggttgggtg	ttttcagggt	ccagtgcctg	gtcagcagct	180
cgtaaaggat	ttccgcgtcc	gtgtccgagg	acagacgtat	atacttccct	ttcttcccca	240
gtgtctcaaa	ctgaatatcc	ccaaaggcgt	cggtaggaaa	ttccttgggt	tgtttcttgt	300
agttccattt	ctcacttttg	ttgatctggg	tgcttccat	gtgctggctc	tgggcatagc	360
cacacttgca	cacattctcc	ctgataagca	cgatgggtgt	gacaggaagg	aaggatttca	420
ttgagcctgc	ttatggaaac	tggtattgtt	agcttaata	gac		463

<210> 363

<211> 653

117

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 363

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ctcttgngga	ttctgggtga	catcttcatg	aatggcaacc	gtgccagwga	ggctgtcctc	120
tgggaggcac	tacgcaagat	gggactgcgt	cctgggggtga	gacatcctct	ccttgagat	180
ctaacgaaac	ttctcaccta	tgagttgtaa	agcagaaata	cctgnactac	agacgagtgc	240
ccaacagcaa	ccccccggaa	gtatgagttc	ctctrgggcc	tccgttccta	ccatgagasc	300
tagcaagatg	naagtgttga	gantcattgc	agagggttcag	aaaagagacc	cntcgtgact	360
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ctgaggccga	agcccgggct	gaagcaagaa	cccgcattgg	aattggagat	gaggctgtgt	480
ntgggccctg	gagctgggat	gacattgagt	ttgagctgct	gacctgggat	gaggaaggag	540
atcttgagaa	tcctnggtcc	agaattccat	ttaccttctg	ggccagatac	caccagaatg	600
cccgctccag	attccctcag	acctttgccg	gtoccattat	tggtcstggt	ggt	653

<210> 364

<211> 401

<212> DNA

<213> Homo sapien

<400> 364

actagaggaa	agacgttaaa	ccaactctact	accacttgtg	gaactctcaa	agggttaaag	60
acaaagccaa	tgaatgactc	taaaaacaat	atttacattt	aatgggtttg	agacaataaa	120
aaaacaaggt	ggatagatct	agaattgtaa	catttttaaga	aaaccatagc	atttgacaga	180
tgagaaagct	caattataga	tgcaaagtta	taactaaact	actatagtag	taaagaaata	240
catttcacac	ccttcatata	aattcactat	cttggcttga	ggcactccat	aaaatgtatc	300
acgtgcatag	taaatcttta	tatttgctat	ggcgttgac	tagaggactt	ggactgcaac	360
aagtggatgc	gcggaaaatg	aaatcttctt	caatagccca	g		401

<210> 365

<211> 356

<212> DNA

<213> Homo sapien

<400> 365

ccagtgtcat	atttgggctt	aaaatttcaa	gaagggcact	tcaaattggct	ttgcatttgc	60
atgtttcagt	gctagagcgt	aggaatagac	cctggcgctc	actgtgagat	gttcttcagc	120
taccagagca	tcaagtctct	gcagcaggtc	attcctgggt	aaagaaatga	cttcacacaa	180
ctctccatcc	cctggctttg	gcttcggcct	tgcgttttcg	gcatcatctc	cgtaaatggt	240
gactgtcacg	atgtgtatag	tacagtttga	caagcctggg	tccatacaga	ccgctggaga	300
acattcggca	atgtcccctt	tgtagccagt	ttcttctctg	agctcccgga	gagcag	356

<210> 366

<211> 1851

<212> DNA

<213> Homo sapien

<400> 366

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cttcgctgtt	cttcattctt	cttcaatagc	cataaatctt	ctagctctgg	ctggctgttt	120
tcacttcctt	taagcctttg	tgactcttcc	tctgatgtca	gctttaagtc	ttgttctgga	180
ttgctgtttt	cagaagagat	ttttaacatc	tggttttctt	tgtagtcaga	aagtaactgg	240

caaattacat	gatgatgact	agaacagca	tactctctgg	ccgtctttcc	agatcttgag	300
aagatacatc	aacattttgc	tcaagtagag	ggctgactat	acttgctgat	ccacaacata	360
cagcaagtat	gagagcagtt	cttccatata	tatccagcgc	atttaaattc	gcttttttct	420
tgattaaaaa	tttcaccact	tgctgttttt	gctcatgtat	accaagtagc	agtgggtgta	480
ggccatgctt	gttttttgat	tcgatatcag	caccgtataa	gagcagtgct	ttggccatta	540
atttatcttc	attgtagaca	gcatagtgta	gagtggtatt	tccatactca	tctggaatat	600
ttggatcagt	gccatgttcc	agcaacatta	acgcacattc	atcttcctgg	cattgtacgg	660
cctttgtcag	agctgtcctc	ttttgtttgt	caaggacatt	aagttgacat	cgtctgtcca	720
gcacgagttt	tactacttct	gaattcccat	tggcagaggc	cagatgtaga	gcagtcctct	780
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cgtctccctg	cagcagggga	agcagtgcca	gcaccacttg	cacctcttgc	tccaagcgt	1020
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gtccatccag	ggaggaagaa	atgcaggaaa	tgaagatgc	atgcacgatg	gtatactcct	1140
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acagaggatg	agatccagaa	accacaatat	ccattcacaa	acaaacactt	ttcagccaga	1260
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ccagtcgcag	agaagccaca	ctgaagctct	gtcctcagcc	atcagcgcca	cggacaggar	1500
tggttttctt	ccccagtgat	gcagcctcaa	gttatcccga	agctgccgca	gcacacggtg	1560
gctcctgaga	aacaccccag	ctcttccggt	ctaacacagg	caagtcaata	aatgtgataa	1620
tcacataaac	agaattaaaa	gcaaagtcac	ataagcatct	caacagacac	agaaaaggca	1680
tttgacaaaa	tccagcatcc	ttgtatttat	tggtgcagtt	ctcagaggaa	atgcttctaa	1740
cttttcccca	tttagtatta	tggtggtgtg	gggcttgcta	tagtggtgtt	ttattacttt	1800
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<210> 367
 <211> 668
 <212> DNA
 <213> Homo sapien

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accrtataag	agcagtgtct	tggccattaa	tttatctttc	attrtagaca	gcrtagtgya	180
gagtggtatt	tccatactca	tctggaatat	ttggatcagt	gccatgttcc	agcaacatta	240
acgcacattc	atcttcctgg	cattgtacgg	cctgtcagta	ttagacccaa	aaacaaatta	300
catatcttag	gaattcaaaa	taacattcca	cagctttcac	caactagtta	tatttaaagg	360
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gcagtcctat	gagagtgaga	agacttttta	ggaaattgta	gtgcactagc	tacagccata	600
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aaaaaaaa						668

<210> 368
 <211> 1512
 <212> DNA
 <213> Homo sapien

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cactgcttcc	cctgctgcag	ggggagtggc	aagagcaacg	tgggcgcttc	tggagaccac	480
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aacaagaagg	acaagcaaaa	gaggactgct	ctacatctgg	cctctgccaa	tgggaattca	780
gaagtagtaa	aactcstgct	ggacagacga	tgtcaactta	atgtccttga	caacaaaaag	840
aggacagctc	tgayaaaagg	cgtacaatgc	caggaagatg	aatgtgcggt	aatgttgctg	900
gaacatggca	ctgatccaaa	tattccagat	gagtattggaa	ataccactct	rcactaygct	960
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tcaaaaaaca	aggtatagat	ctactaattt	tatcttcaaa	atactgaaat	gcattcattt	1080
taacattgac	gtgtgtaagg	gccagtcttc	cgtatttggg	agctcaagca	taacttgaat	1140
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agaagcatta	gagggtagac	tttttttttt	ttaaatgcac	ttctggtaaa	tacttttggt	1260
gaaaacactg	aatttgtaaa	aggtaatact	tactattttt	caatttttcc	ctcctaggat	1320
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actccaagaa	aagttaaaca	tgtttcagtg	aatagagatc	ctgctccttt	ggcaagttcc	1440
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tgatctcgtg	cc					1512

<210> 369

<211> 1853

<212> DNA

<213> Homo sapien

<400> 369

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ttcaaacaga	ttggaaaccc	ggagttacct	gctagttggt	gaaactgggt	ggtagacgcg	180
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tccatgcggg	ctgcttcttc	tgtgaagaag	ccatttgggtc	tcaggagcaa	gatgggcaag	300
tgggtgctgcc	gttgcttccc	ctgctgcagg	gagagcggca	agagcaacgt	gggcacttct	360
ggagaccacg	acgactctgc	tatgaagaca	ctcaggagca	agatgggcaa	gtggtgccgc	420
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120

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<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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<210> 373

<211> 1155

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<212> DNA

<213> Homo sapien

<400> 373

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<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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123

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<210> 375

<211> 2040

<212> DNA

<213> Homo sapien

<400> 375

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<211> 329

<212> PRT

<213> Homo sapien

<400> 376

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His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
      115      120      125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
      130      135      140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
      145      150      155      160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
      165      170      175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
      180      185      190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
      195      200      205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
      210      215      220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
      225      230      235      240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
      245      250      255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
      260      265      270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
      275      280      285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
      290      295      300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
      305      310      315      320
Ser Met Leu Phe Leu Val Ile Ile Met
      325

```

<210> 377
 <211> 148
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(148)
 <223> Xaa = Any Amino Acid

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<400> 377
Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
  1      5      10      15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
      20      25      30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
      35      40      45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu

```

125

50		55		60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp				
65		70		75
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp				
	85		90	
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro				
	100		105	
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp				
	115		120	
Lys Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser				
	130		135	
Lys Asn Lys Val				
145				

<210> 378

<211> 1719

<212> PRT

<213> Homo sapien

<400> 378

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys				
1		5		10
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe				
	20		25	
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp				
	35		40	
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp				
	50		55	
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val				
65		70		75
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn				
	85		90	
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser				
	100		105	
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe				
	115		120	
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His				
	130		135	
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met				
145		150		155
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala				
	165		170	
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu				
	180		185	
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr				
	195		200	
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met				
	210		215	
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn				
225		230		235
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys				
	245		250	
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly				
	260		265	
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val				
	275		280	
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr				
	290		295	
			300	

126

Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355					360					365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys
	370					375					380				
Pro	Arg	Thr	His	Met	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	
385					390				395					400	
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys
				405					410					415	
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly
			420					425					430		
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys
		435					440						445		
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly
	450					455					460				
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys
465					470					475					480
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys
			485						490					495	
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp
			500					505					510		
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu
		515					520						525		
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp
	530					535						540			
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln
545					550					555					560
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val
			565						570					575	
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn
			580					585					590		
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu
		595					600					605			
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp
	610						615					620			
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys
625					630					635					640
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys
			645						650					655	
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	
			660				665						670		
Gln	Gln	Val	Val	Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala
		675					680					685			
Leu	Asp	Arg	Tyr	Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly
	690					695					700				
Ser	Ala	Ser	Ile	Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser
705					710					715					720
Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser
			725						730					735	
His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln
			740					745					750		
Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys
		755					760						765		

Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser
 770 775 780
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp
 785 790 795 800
 Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly
 805 810 815
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn
 820 825 830
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe
 835 840 845
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser
 850 855 860
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn
 865 870 875 880
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu
 885 890 895
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile
 900 905 910
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn
 915 920 925
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro
 930 935 940
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu
 945 950 955 960
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe
 965 970 975
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His
 980 985 990
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser
 995 1000 1005
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu
 1010 1015 1020
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His
 1025 1030 1035 1040
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met
 1045 1050 1055
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met
 1060 1065 1070
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys
 1075 1080 1085
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr
 1090 1095 1100
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys
 1105 1110 1115 1120
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp
 1125 1130 1135
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His
 1140 1145 1150
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp
 1155 1160 1165
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg
 1170 1175 1180
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val
 1185 1190 1195 1200
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys
 1205 1210 1215
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly
 1220 1225 1230

128

Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn
 1235 1240 1245
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys
 1250 1255 1260
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro
 1265 1270 1275 1280
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr
 1285 1290 1295
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp
 1300 1305 1310
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val
 1315 1320 1325
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala
 1330 1335 1340
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala
 1345 1350 1355 1360
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn
 1365 1370 1375
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr
 1380 1385 1390
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr
 1395 1400 1405
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu
 1410 1415 1420
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly
 1425 1430 1435 1440
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn
 1445 1450 1455
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser
 1460 1465 1470
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly
 1475 1480 1485
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu
 1490 1495 1500
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys
 1505 1510 1515 1520
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser
 1525 1530 1535
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu
 1540 1545 1550
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser
 1555 1560 1565
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe
 1570 1575 1580
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe
 1585 1590 1595 1600
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly
 1605 1610 1615
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro
 1620 1625 1630
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln
 1635 1640 1645
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile
 1650 1655 1660
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser
 1665 1670 1675 1680
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn
 1685 1690 1695

129

Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr
 1700 1705 1710
 Met Lys His Gln Ser Gln Leu
 1715

<210> 379
 <211> 656
 <212> PRT
 <213> Homo sapien

<400> 379
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu

130

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      370      375      380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385      390      395      400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
      405      410      415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
      420      425      430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
      435      440      445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
      450      455      460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465      470      475      480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
      485      490      495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
      500      505      510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
      515      520      525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
      530      535      540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545      550      555      560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
      565      570      575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
      580      585      590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
      595      600      605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
      610      615      620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625      630      635      640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
      645      650      655

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<210> 380
<211> 671
<212> PRT
<213> Homo sapien

```

```

<400> 380
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1      5      10      15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20      25      30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35      40      45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
      50      55      60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65      70      75      80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85      90      95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100      105      110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115      120      125

```

131

Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
130						135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
			165						170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180					185					190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
	195						200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
210						215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
			245						250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275					280					285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
290						295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355				360						365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
370					375						380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395					400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
			420					425					430		
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
		435					440					445			
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
450						455					460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470					475					480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485					490					495	
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
			500					505					510		
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp
							520					525			
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys
530						535					540				
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala
545					550					555					560
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg
				565					570					575	
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His
				580				585						590	

132

Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
 595 600 605
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
 610 615 620
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys
 625 630 635 640
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala
 645 650 655
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 660 665 670

<210> 381
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 381
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa 60
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcacatgac ctctgagggg 120
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggacca ggactcacac 180
 atcctggggc tccaaggcag aggagagggt cctcaagaag gtcaggagga aaatccgtaa 240
 caagcagtca g 251

<210> 382
 <211> 3279
 <212> DNA
 <213> Homo sapiens

<400> 382
 ctctctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120
 cactgggagg ggacatcctg cagaaggtag gagttagcaa acaccgctg caggggaggg 180
 gagagccctg cggcacttg gggagcagag ggagcagcac ctgcccaggc ctgggagggg 240
 gggcctggag gccgtgagga ggagcgagg ggctgcatgg ctggagttag ggatcagggg 300
 cagggcgcgga gatggcctca cacagggaag agaggggccc tctgagagg cctcacctgg 360
 gccacaggag gacactgctt ttcctctgag gagtacaggag ctgtggatgg tgctggacag 420
 aagaaggaca gggcctggct caggtgtcca gaggtgtcgt ctggcttccc tttgggatca 480
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
 gtggctccag gccttgcccc tgctggggc ctcacccagc ctccctcaca gtctcctggc 600
 cctcagtcct tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660
 gaactgacca taccagccc tgcccacggc cctccatggc tcccgaatgc cctggagagg 720
 ggacatctag tcagagagta gtctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
 gcacactgca gatggtccc gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840
 ggaccttgcc ccttgtgcag gagctggacc ctgaagtccc ctcccatag gccaaactg 900
 gagccttggt cctctgttg gactccctgc ccatattctt gtgggagtgg gttctggaga 960
 catctctgtc tgttcctgag agctgggaat tgcctcagtc catctgcctg cgcggttctg 1020
 agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140
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 gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgc ccctgtccca 1260
 ccctacctc tagtaaatat aagtccacct cacgttctgg catcacttgg cctttctgga 1320
 tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gagtccctact 1380
 gacctgtgct ttctgggtgt gagtccaggg ctgctaggaa aaggaatggg cagacacagg 1440
 tgtatgcaa tgtttctgaa atgggtataa tttcgtctc tcttcggaa cactggctgt 1500
 ctctgaagac ttctcgctca gtttcagtga gacacacac aaagacgtgg gtgacctgt 1560
 tgtttgtggg gtgcagagat gggaggggtg gggccacccc tggagagtg gacagtga 1620
 caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680
 acacacagca aggttgacgc tgtaaacata gccacgctg tctggggggc actgggaagc 1740

```
<210> 383
<211> 154
<212> PRT
<213> Homo sapiens
```

```
<210> 384
<211> 557
<212> DNA
<213> Homo sapiens
```

<400> 384

```
ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaagggg cccttttgca ttgccaagtg ccataacat gagcactact ctaccatggg 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccaggacact tggaaacagt tggcactgta aggtgcttgc 360
tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540
aaaaaaaaa aaaaaaa 557
```

<210> 385

<211> 337

<212> DNA

<213> Homo sapiens

<400> 385

```
ttcccagggtg atgtgcgagg gaagacacat ttactatcct tgatgggggt gattccttta 60
gtttctctag cagcagatgg gttaggagga agtgaccaa gtggttgact cctatgtgca 120
tctcaagacc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt cctgtcgtg gtctggatct 300
ctttggccac caattcccc tttccacat cccggca 337
```

<210> 386

<211> 300

<212> DNA

<213> Homo sapiens

<400> 386

```
gggcccgtc cggcccagg cccgcctcg cgagtcctcc tccccgggtg cctgcccga 60
gcccgctcgg ccagaggggt gggcgcgagg ctgcctctac cggttgagg ctgtaactca 120
gcgaccttgg ccgaagggt ctagcaagga ccaccgacc ccagccggg cggcggggc 180
gcggactttg cccggtgtgt gggcgggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300
```

<210> 387

<211> 537

<212> DNA

<213> Homo sapiens

<400> 387

```
gggcccagtc gggcaccaag ggactctttg caggcttctt tcctcggatc atcaaggctg 60
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggtctctg ggcggtgaa aggggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttcttc agcactgagg 240
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggtt gtccctctgg 300
gcggcccagc acttctcag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360
cttaccacc cccaagtgc aagacaaat cttccagctg ccccttctgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctacgcctgg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaaa 537
```

<210> 388

<211> 520

<212> DNA

<213> Homo sapiens

135

```

<400> 388
aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggttaaa ccagtttgca ttcccctaag gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaatttgtt tatttcactt gccaaagtga 180
ggacccccct cccaacatgc ccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttggt gacctacca gagaccagga gggtttggtt agctcacagg 300
acttcccca cccagaaga ttagcatccc atactagact cataactaac tcaactaggc 360
tcatactcaa ttgatgggta ttagacaatt ccatttcttt ctgggttatta taaacagaaa 420
atctttcttc ttctcattac cagtaaaggc tcttggtatc tttctggttg aatgatttct 480
atgaacttgt cttattttta tgggtgggtt ttttcttggt 520

```

```

<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

```

```

<400> 389
cggtgcccc gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcaccgct ctgctctcac agctgagact 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggctgtgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aaggggtgctg 360
gggag 365

```

```

<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

```

```

<400> 390
tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgctg ttccaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

```

```

<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

```

```

<400> 391
tgagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgcag tctctaccta ccagtacgat 300

```

136

gagacctccg gctactacta tgacc

325

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(277)

<223> n = A,T,C or G

<400> 392

```

atattgttta actccttcct ttatatcttt taacattttc atggngaaa gttcacatct 60
agtctcactt nggcnagn gn ctcctacttg agtctcttcc ccggcctggn ccagtngnaa 120
antaccanga accgncatgn cttanaaanc ncctgggttn tgggttnntc aatgactgca 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

```

<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

```

actagtccag tgtggtggaa ttgcggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga tttaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggctt agtttgtcca tcagcattat catgatata ggactggtta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttgga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcctcctgta aacattttat 360
cattatttaa tcctccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgccttctgt tttgctagtt tgtgttgttg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
tttgcctat caaaaaaaaa aaaaaa 566

```

<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

```

gaacatacat gtcccgccac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tccaagatt atcgggagaa agggggcagt aattaccaa atccggttg agcatgacgt 240
gaacatccag tttctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag gtagctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384

```

<210> 395

<211> 399

<212> DNA

137

<213> Homo sapiens

<400> 395

```

ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacgg 360
gcagcctggg gagaccatcc aatcccaa 399

```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```

tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtggag gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgtag gccctgctct ttt 403

```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

```

actagtnacg tgtggtggaa ttcgcgccg cgtcgacctc naanccatct ctatagcaaa 60
tccatccccg ctctggttg gtnacagaat gactgacaaa 100

```

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398

```

ggggccgcgt cgacagcagt tccgccagcg ctgcccctg ggtggggatg tgctgcacgc 60
ccactgggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggagg actcatcatg 180

```


138

ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
 ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399
 <211> 298
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(298)
 <223> n = A,T,C or G

<400> 399
 acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
 ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcggtgggct 120
 ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcatgggct 180
 ccggcattga gcgcatgggc ccgctgggcc togaccacat ggcctccanc attgancgca 240
 tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400
 <211> 548
 <212> DNA
 <213> Homo sapiens

<400> 400
 acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatcccctt ttcctgcctt 60
 gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
 caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
 tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
 tgcagagggc tagagaatta tttcatacag gctttgaggc caccatgtc acttatcccg 300
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
 gttggcccca taattctggg cctttgttgt ttgttttaac tacttgggca tccaggaag 420
 ctttccagtg atctctacc atgggcccc ctccctgggat caagcccctc ccaggccctg 480
 tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tccattggg 540
 agcaggtt 548

<210> 401
 <211> 355
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(355)
 <223> n = A,T,C or G

<400> 401
 actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
 tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
 taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
 tataaatgaa tgtgtggaag caaagtggcc atggtggcgg cgaagaagan aaagatgtgt 240
 tttgttttgg actctctgtg gtcccttcca atgctgnngg tttccaacca ggggaaggg 300
 cccttttgca ttgccaagtg ccataacat gagcactact ctaccatggn tctgc 355

<210> 402
 <211> 407
 <212> DNA

139

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

```
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag cagggtgttc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaagggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa ttgctgagg 300
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407
```

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

```
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaattc aggcacccaa 60
tcctaagcaa gagcctatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcattgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattattttac ataaacctcc attcggtaac catgttgaaa 300
gga 303
```

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

```
aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtgc tctcttgatc ctacaaacag 120
acattttcca ctctgttttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225
```

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaatt ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
```

140

tcatcccat cccatgccaa aggaagacc tccctccttg gctcacagcc ttctctaggc 180
ttccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcannng tggatcccac ccct 334

<210> 406
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216

<210> 407
<211> 413
<212> DNA
<213> Homo sapiens

<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcaccagtg tgcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccattgta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413

<210> 408
<211> 183
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G

<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggtan ntaatcctta actagtccct ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt 183

<210> 409
<211> 250
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature

141

<222> (1)...(250)

<223> n = A,T,C or G

<400> 409

```

cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtgggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt totcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
ggcctatgc                                     250

```

<210> 410

<211> 306

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(306)

<223> n = A,T,C or G

<400> 410

```

ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tccatttgc aggatccgtc tgtgcacatg cctotgtaga gagcagcatt 120
cccaggggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaaga cacatcctaa 180
aagggtgtgt aatggtgaaa accgcttcct tctttattgc ccttcttat ttatgtgaac 240
nactggttg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc                                     306

```

<210> 411

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(261)

<223> n = A,T,C or G

<400> 411

```

agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggngaggcaa a                                     261

```

<210> 412

<211> 241

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```

gttcaatgtt acctgacatt tctacaacac ccactcacc gatgtattcg ttgccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt ctgcccagc aaatactacg 120

```

142

actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcaactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241

<210> 413
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 413
aactcttaca atccaagtga ctcactctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtag cttctctttg ttgtgaagga taatcaaaact gaacaacaaa 120
aagtttactc tcttcatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414
<211> 234
<212> DNA
<213> Homo sapiens

<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca 234

<210> 415
<211> 217
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(217)
<223> n = A,T,C or G

<400> 415
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcactttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416
<211> 213
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416

143

```

atgcataatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag                                     213

```

<210> 417

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 417

```

nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaadc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt                                     303

```

<210> 418

<211> 328

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 418

```

tttttgccg tgggtggggca gggacggggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgtctan gattacaggc cgtgagcc                                     328

```

<210> 419

<211> 389

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(389)

<223> n = A,T,C or G

<400> 419

```

cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatag 60
accctgagc catggactgg agcctgaaag gcagcgta ca cctgctcct gatcttgctg 120
cttgtttcct ctctgtggct ccattcatag cacagttgtt gcaactgagg ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360

```

tggcagccac tcnggctgtg tcgacgcgg

389

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```
gttcctccta actcctgcc aaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccagggc agcaagcctt agccttggt tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtccattga cacctttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcctgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccg 408
```

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```
gtcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnata acttgacgtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatctctg tttcgtagca agtgcctgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttctt gg 352
```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```
atgccaccat gctggcaatg cagcgggagg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcgggcg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcgggcgg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgcg attcaccgac 300
gcttcttcgg ccggtacggc tggcctatga aaattat 337
```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(310)

<223> n = A,T,C or G

<400> 423

145

```

gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggccctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcaactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta                                     310

```

<210> 424

<211> 370

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(370).

<223> n = A,T,C or G

<400> 424

```

gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acagggtctt tttgggtcct ttcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcatgtgta taagcaggac 360
tccgtcgacg                                     370

```

<210> 425

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 425

```

aattgctatn ntttattttg ccaactcaaaa taattaccaa aaaaaaaaaa tnttaaata 60
taacaacnca acatcaaggc aananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggnatagc acacagacaa acatgcccag 180
gaggnnttca ggaccgctcg atgtnttntg aggagg                                     216

```

<210> 426

<211> 596

<212> DNA

<213> Homo sapiens

<400> 426

```

cttcagtgga ggataaccct gttgccccgg gccgagggtc tccattaggc totgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gotttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgtggtg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

```


146

<210> 427
 <211> 107
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(107)
 <223> n = A,T,C or G

<400> 427
 gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
 cccgggagca gccttanaga gtcctgttt gactgccggg ctcagng 107

<210> 428
 <211> 38
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(38)
 <223> n = A,T,C or G

<400> 428
 gaacttocna anaangactt tattcactat ttacatt 38

<210> 429
 <211> 544
 <212> DNA
 <213> Homo sapiens

<400> 429
 ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
 attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
 atatccacga actcttgaag gactttctga tttatocaca atcaaatcat cggttttcag 180
 tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactogtt 240
 gccttccact tcagttacac ctcaactcacc atcctctcct gttggttctg tgcgtcttca 300
 agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
 tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
 gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
 acctcaacaa gtttagagaga tatgcataac cagggatttt ttgccagggtg gtaggagaga 540
 ttat 544

<210> 430
 <211> 507
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(507)
 <223> n = A,T,C or G

<400> 430
 cttatcncaa tgggggtccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
 gaacactgac acccatcttc caccgccgaca ctctgattta attgggctgc agtgagaaca 120

147

```

gagcatcaat ttaaaaagct gccagaatg ttntoctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggg ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtcaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcttc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507

```

```

<210> 431
<211> 392
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtctggggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct 392

```

```

<210> 432
<211> 387
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G

```

```

<400> 432
ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgna gtccagccac tgnгааacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tatcttctgt ctgtctgnga 240
attctgttgc ttctggggca ttctcttng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgta aggaccggga 360
acaacgtata gaacactgga gtccttt 387

```

```

<210> 433
<211> 281
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G

```

```

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60

```

148

```

ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atgcgcgtgg ctattcctcn ttgntattac accagnaggg ntctctgtnt gccacttggg 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```

ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcacaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaacctt ttcaccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484

```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```

gcgccgctca gagcaggtea ctttctgcct tccacgtcct ccttcaagga agcccatgt 60
gggtagcttt caatctgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcaggtgtc ggggtgacc 240
cttgagaga ggaagaggc cacaagaggg gctgccaccg ccactaacgg agatggcct 300
ggtagagacc tttgggggtc tggaaacctt ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaacctt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424

```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

```

accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtaacgt ctgtgcttgc aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540
accaaaagtc caaacttcaa ctcttggct agtacacttc ggtctagcca gaaaaaagc 600
agaacaaga agccaaggct aaggcttgct gcctgccag gaggggggt gcagctctca 660

```

149

tggttgag

667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc aactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attccttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggctactcct ctatcttcac cctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc ttttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgttg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc                                     693

```

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgaggagg ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggtccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

```

gttcctnnta actcctgcc aaaaacagctc tctcaacat gagagctgca cccctcctcc 60
tgccaggggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacccttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag t                                     431

```

<210> 440

<211> 523

<212> DNA

<213> Homo sapiens

150

<400> 440

```
agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcctttt tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcactctga tgagaacaag cta 523
```

<210> 441

<211> 430

<212> DNA

<213> Homo sapiens

<400> 441

```
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccaggggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggg gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attccttgaat gagtctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag 430
```

<210> 442

<211> 362

<212> DNA

<213> Homo sapiens

<400> 442

```
ctaaggaatt agtagtggtc ccataccttg tttggagtg gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtagggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatott ttattgcact tgttttgacc attagctat 180
atgttttagaa atgggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362
```

<210> 443

<211> 624

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(624)

<223> n = A,T,C or G

<400> 443

```
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaacttg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
```

151

```

taacgcctac aaaacactta aacatagata acatagggtgc aagtactatg tatctgggtac 420
atggtaaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga ggggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc 624

```

```

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

```

```

<400> 444
gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacctgtg gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa ttagtagtag 420
gtaga 425

```

```

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

```

```

<400> 445
catgttttatg nttttggatt actttgggca cctagtgttt ctaaatogtc tatcattcctt 60
ttctgtttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcatgtggc agattattgg atgtagtctt cttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggtttotcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcaattta gtag 414

```

```

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120

```

152

```

atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaactttc caaccttcca ggaaatgcc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatggt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgcttg catttggtgt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatattga 600
aatagtatac attgtcttga tgttttttct g 631

```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```

ccttgggaaa antntcacia tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtc ggtcaacgtc tgtgcttoga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtca gtacacttcg gtcta 585

```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```

tgctcgtggg tcattctgan nnccgaactg acctgcccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93

```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(706)

<223> n = A,T,C or G

<400> 449

```

ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60

```

153

```

ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggctcggcg cgctccattc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgtctattac ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc caggggtttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct cttagcgggc cgctactac tactaaattc gcggcgcgct 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706

```

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

```

gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcagggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcgggc 480
gcgaatttag tag 493

```

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 451

```

gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cgggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg ggcatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttccagc cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
tgagagtgga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncacagc actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtggag 420
gttgcaatga gctgagatca ggconctgcn cccacagcat gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(51)

<223> n = A,T,C or G

154

<400> 452
 agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453
 <211> 317
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(317)
 <223> n = A,T,C or G

<400> 453
 tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaaccat 120
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
 taacaaaccc tgtccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
 taccatgtc tttatta 317

<210> 454
 <211> 231
 <212> DNA
 <213> Homo sapiens

<400> 454
 ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
 taagccacgc cagctctctg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
 agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
 cttcctttt tcagtgttcc aaagctctc acaatttcat gaacaacagc t 231

<210> 455
 <211> 231
 <212> DNA
 <213> Homo sapiens

<400> 455
 taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60
 cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
 gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
 caaagaattt ctcatagcac agctcacaat acagggtcc tttctcctct a 231

<210> 456
 <211> 231
 <212> DNA
 <213> Homo sapiens

<400> 456
 ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
 ttccattcag tattatcggtt attattcttg gagaaacct gtctgtttac tgtaaccttt 120
 tgactcaaaa ttcctttatc aggaataact acatagccac tattacaaa gccattggaa 180
 cttttttatt tgggtcagct gctagtcagt ccctgactga cattgccaag t 231

<210> 457
 <211> 231
 <212> DNA

155

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

```
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatTTTTtctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g 231
```

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

```
aggtctggtt cccccactt ccactcccct ctactctctc taggactggg ctgggccaaag 60
agaagagggg tggttaggga agcogttgag acctgaagcc ccacctcta ccttccttca 120
acaccctaac cttgggtaac agcatttga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231
```

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

```
ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231
```

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

```
gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaa 120
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a 231
```

<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

```
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgccctg tgtgtcctgg 120
gtggggttca gtgaggagtg ggaaattggg tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231
```

<210> 462

156

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

```
aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtattttaatt tcttctcact catccagtgt tgtatttagg a 231
```

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

```
tactccagcc tggtgacaga gcgagaccct atcaccgccc cccacccccc caaaaaaaaa 60
actgagtaga caggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120
catttgacag gtgtcttttc ctctggacct cgggtgcccc atctgagtga gaaaaggcag 180
tggggagggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c 231
```

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

```
gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgaact 60
aaggacatca catatgaaga atgtttaagt tggagggtggc aacgtgaatt gcaaacaggg 120
cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgccagcg caccagctag atgctctgta acttctaggg cccattttcc c 231
```

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

```
catgttggtg tagctgtggt aatgctggct gcatctcaga cagggttaac ttcagctcct 60
gtggcaaatt agcaacaaat tctgacatca tatatatggt ttctgtatct ttgttgatga 120
aggatggcac aatttttgct tgtgttcata atatactcag attagtccag ctccatcaga 180
taaactggag acatgcagga cattagggtg gtgtttagtc tctggtaatg a 231
```

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

```
caggtaacctc tttccattgg ataactgtgct agcaagcatg ctctccgggg tttttttaat 60
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaactt ttgccagga 120
cctgtgcaat caaatattgt ggagaattcc ctgactggag aagtcacaaa gactataggc 180
aataatggag accagtccca caagatgaca accagtcggt gtgtgcggt g 231
```

<210> 467

<211> 311

<212> DNA

<213> Homo sapiens

<400> 467

```

gtacaccctg gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg 60
tggtggcctt tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac 120
tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggtgtg ggacgtcagt 240
tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
ctgcagcaga c                                     311

```

<210> 468

<211> 3112

<212> DNA

<213> Homo sapiens

<400> 468

```

cattgtgttg ggagaaaaac agaggggaga tttgtgtggc tgcagccgag ggagaccagg 60
aagatctgca tgggtgggaag gacctgatga tacagagttt gataggagac aattaaaggc 120
tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180
atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtggttcaa 240
cgaggacttg gaattgcatg gagctggagc tgaagttag cccaattgtt tactagttag 300
gtgaatgttg atgattggat gatcatttct catctctgag cctcaggttc cccatccata 360
aaatgggata cacagtatga tctataaagt gggatatagt atgatctact tccctgggtt 420
atgtgaagga tgaattgaga taatttatit cagggtgccta gaacaatgcc cagattagta 480
catttgggtg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540
gattatcatt caatctcata gttttgtcat ggcccaattt atcctcactt gtgcctcaac 600
aaattgaact gtttaacaaag gaatctcttg tctgggttaa tggctgagca ccactgagca 660
tttccattcc agttggcctt ttgggtttgc tagctgcac actagtcac ttaaataaat 720
gaagttttaa catttctcca gtgattttt tatctcacct ttgaagatac tatgttatgt 780
gattaaataa agaacttgag aagaacaggt ttcattaaac ataaaatcaa tgtagacgca 840
aattttctgg atgggcaata cttatgttca caggaaatgc tttaaaatat gcagaagata 900
attaaatggc aatggacaaa gtgaaaaact tagacttttt tttttttttt ggaagtatct 960
ggatgttcct tagtcactta aaggagaact gaaaaatagc agtgagttcc acataatcca 1020
accttgagga ttaaggctct ttgtggggaa ggacaaagat ctgtaaaatt acagtttcc 1080
tccaaagcca acgtgcaatt ttgaaacata tcaaagctct tcttcaagac aaataatcta 1140
tagtacatct ttcttatggg atgcacttat gaaaaatggt ggctgtcaac atctagtcac 1200
tttagctctc aaaatggttc attttaagag aaagttttag aatctcatat ttattcctgt 1260
ggaaggacag cattgtggct tggactttat aaggctttta ttcaactaaa taggtgagaa 1320
ataagaaagg ctgctgactt taccatctga ggccacacat ctgctgaaat ggagataatt 1380
aacatcacta gaaacagcaa gatgacaata taatgtctaa gtagtacat gtttttgac 1440
atttccagcc cctttaaata tccacacaca caggaagcac aaaaggaagc acagagatcc 1500
ctgggagaaa tggccggccg ccatcttggg tcatcgatga gcctcgccct gtgcctggct 1560
ccgcttgtga ggaaggaca ttgaaaaatg aattgatgtg ttccttaaag gatgggcagg 1620
aaaacagatc ctgttgtgga tatttatitg aacgggatta cagatttgaa atgaagtcac 1680
aaagtgagca ttaccaatga gaggaaaaca gacgagaaaa tcttgatggc ttcacaagac 1740
atgcaacaaa caaaatggaa tactgtgatg acatgaggca gccagctgg ggaggagata 1800
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<210> 469

<211> 2229

<212> DNA

<213> Homo sapiens

<400> 469

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<211> 2426

<212> DNA

<213> Homo sapiens

<400> 470

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<211> 812

<212> DNA

<213> Homo sapiens

<400> 471

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160

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<211> 515

<212> DNA

<213> Homo sapiens

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<400> 472

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<210> 473

<211> 5829

<212> DNA

<213> Homo sapiens

<400> 473

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<210> 474

<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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aaaatataaa tatatagaca tctcagataa tatatttgaa atagcaaatt cctgttagaa 180
aataatagta cttaactaga tgagaataac aggtcgccat tatttgaatt gtctcctatt 240
cgtthtttcat ttgttggtgt actcatgttt tacttatgag ggatatatat aacttccact 300
gttttcagaa ttattgtatg cagtcagtat gagaatgcaa tttaagtthc cttgatgctt 360
tttcacactt ctattactag aaataagaat acagtaatat tggcaaaaga aattgaccag 420
ttcaataaaa tthtttagta aatctgattg aaaataaaca ttgcttatgg ctttcttaca 480
tcaatattgt tatgtcctag acacctatc tgaaattacg gcttcaaat tctaattatg 540
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gctgagagag aaagatgcta gctccgcaag ccggagaggg aacaccgcca cattgttaca 660
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gaagggaaga ggctggggc tggagtattc gctt 1594

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<210> 475

<211> 2414

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (33)

<223> n=A,T,C or G

<400> 475

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gcttcttgat ttgtaaaatt ctatgtcatt ggctcaaatt tgtatagtat ctcaaaatat 300
aaatatatag acatctcaga taatatattt gaaatagcaa attcctgtta gaaaataata 360
gtacttaact agatgagaat aacaggctgc cattatttga attgtctcct attcgttttt 420
catttggtgt gttactcatg ttttacttat ggggggatat atataacttc cgctgttttc 480
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<210> 476

<211> 3434

<212> DNA

<213> Homo sapiens

<400> 476

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tgccaaggag ccagccacag gtcacattga ggaggacttt atgttccagt ccagaaaagca 180
gccagtggta ccacccaggg gacttgtgct tctgtggccc aggccagacg tagaatttga 240
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```

<210> 477

<211> 140

<212> PRT

<213> Homo sapiens

165

<400> 477

```

Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro
                    5                      10                      15
His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
                20                      25                      30
Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
                35                      40                      45
His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
                50                      55                      60
His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
                65                      70                      75                      80
Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
                85                      90                      95
Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
                100                      105                      110
Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
                115                      120                      125
Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
                130                      135                      140

```

<210> 478

<211> 143

<212> PRT

<213> Homo sapiens

<400> 478

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Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5                      10                      15
Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20                      25                      30
Gly Glu Ile Thr Trp Thr His His Thr Ile Thr Gly Thr Gln Thr
                35                      40                      45
His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
                50                      55                      60
Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
                65                      70                      75                      80
Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
                85                      90                      95
His Gly His Thr Ser Thr Pro Ser His His Thr His Cys Leu Trp
                100                      105                      110
Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
                115                      120                      125
His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
                130                      135                      140

```

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

```

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5                      10                      15
Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20                      25                      30

```

166

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
 35 40 45
 His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
 50 55 60
 Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
 65 70 75 80
 Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
 85 90 95
 His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
 100 105 110
 Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
 115 120 125
 Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
 130 135 140
 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
 145 150 155 160
 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
 165 170 175
 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
 180 185 190
 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
 195 200 205
 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
 210 215 220

<210> 480

<211> 144

<212> PRT

<213> Homo sapiens

<400> 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
 5 10 15
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
 20 25 30
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
 35 40 45
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
 50 55 60
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
 65 70 75 80
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
 85 90 95
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
 100 105 110
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
 115 120 125
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
 130 135 140

<210> 481

<211> 167

<212> PRT

<213> Homo sapiens

<400> 481

167

[illegible]

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<210> 482
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 482																
Met	Glu	Pro	Tyr	Arg	Gly	Asn	Lys	Lys	Gln	Val	Gln	Glu	Lys	Gly	Val	
				5					10					15		
Pro	Cys	Leu	Trp	Gly	Ser	Ser	Pro	Cys	Leu	Arg	Cys	His	Met	Ala	Leu	
			20					25					30			
Arg	Ala	Ser	Trp	Leu	Pro	Gly	Gly	Gly	Pro	Gln	Ala	Ile	Leu	Gly	Arg	
		35					40					45				
Thr	Leu	Cys	Ser	Ser	Ala	Glu	Ser	Ser	Gln	Asp	Cys	His	Pro	Gly	Gly	
	50					55					60					
Pro	Ser	Ile	Ala	Leu	Ala	Lys	Pro	Cys	Arg	Gly	Val	Trp	Leu	Leu	Phe	
	65				70					75					80	
Glu	Pro	Ala	Trp	Pro	Pro	Trp	His	Ala	Arg	Ala	Pro	Gly	Ala	Gly	Thr	
				85					90					95		
Leu	Leu	Arg	Val	Cys	Leu	Ser	Cys	Leu	Gly	Cys	His	Leu	Cys	Gly	Gly	
		100						105				110				
Ala	Ser	Gly	Gly	Gly	Gly	Pro	Ala	Thr	Asn	Leu	Thr	Gln	Ser	Arg	Lys	
		115				120						125				
Trp	Met	Ala	Met	Phe	Pro	Gln	Pro	Glu	Trp	Leu	Pro	Pro	Asp	Gly		
	130					135					140					

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<210> 483
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 483
Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5                      10                      15
Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala

```

168

20 25 30
 Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
 35 40 45
 Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
 50 55 60
 Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
 65 70 75 80
 Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
 85 90 95
 Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
 100 105 110
 Arg Leu Val Gln Ala Glu His Pro Pro His Pro Leu Glu Glu Val
 115 120 125
 Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
 130 135 140

<210> 484
 <211> 30
 <212> PRT
 <213> Homo Sapien

<400> 484
 Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
 1 5 10 15
 Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
 20 25 30

<210> 485
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 485
 gggaagctta tcacctatgt gccgcctctg c

31

<210> 486
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 486
 gcgaattctc acgctgagta ttggtgcc

27

<210> 487
 <211> 36
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 487

169

cccgaaattct tagctgccca tccgaacgcc ttcac

36

<210> 488
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 488
 gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489
 <211> 19
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 489
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
 1 5 10 15
 Ser Val Ala

<210> 490
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 490
 Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
 1 5 10 15
 Leu Ser His Ser
 20

<210> 491
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 491
 Thr Cys Leu Ser His Ser Val Ala Val Thr Ala Ser Ala Ala Leu
 1 5 10 15
 Thr Gly Phe Thr
 20

<210> 492
 <211> 20
 <212> PRT

170

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 495

Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu	Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro
1				5					10					15	
Phe	Pro	Asn	Gly												
			20												

<210> 496

<211> 21

<212> PRT

<213> Artificial Sequence

171

<220>

<223> Made in a lab

<400> 496

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

<210> 497

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 497

Leu	Leu	Pro	Pro	Pro	Pro	Ala	Leu	Cys	Gly	Ala	Ser	Ala	Cys	Asp	Val
1				5				10						15	
Ser	Val	Arg	Val												
				20											

<210> 498

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 498

Asp	Val	Ser	Val	Arg	Val	Val	Val	Gly	Glu	Pro	Thr	Glu	Ala	Arg	Val
1				5				10						15	
Val	Pro	Gly	Arg												
				20											

<210> 499

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5				10						15	
Ser	Ala	Phe	Leu												
				20											

<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

172

<223> Made in a lab

<400> 500

Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met
 1 5 10 15
 Gly Ser Ile Val
 20

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met
 1 5 10 15
 Val Ser Ala Ala
 20

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(414)

<223> n=A,T,C or G

<400> 502

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tcagtccgtg	gaggagtcog	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
agggaagggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnattt	ccaaaacctn	gaccacggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatTTTTTg	tggcagaatg	aatactggta	atagtggttg	360
gaagaatatt	tggggcccag	gcaccctggt	caccgtntcc	tcagggaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(379)

<223> n=A,T,C or G

<400> 503

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agctatggag	tgagctgggt	ccgccaggct	ccagggaagg	ggctggnata	catcggatca	180
ttagtagtag	tggtagattt	tacgcgagct	gggcgaaagg	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	aggggggttt	aattataaag	acatttgggg	cccaggcacc	ctgggtcaccg	360

tntccttagg gcaacctaa

379

<210> 504
 <211> 19
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 504
 Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu
 1 5 10 15
 Asn Ser Ala

<210> 505
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 505
 Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr
 1 5 10 15
 Asn Thr Ala Asn
 20

<210> 506
 <211> 407
 <212> DNA
 <213> Homo Sapien

<400> 506
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 accgtctctg gattctccct cagtagcaat gcaatgatct gggcccgcca ggctccaggg 180
 aaggggctgg aatacatcgg atacattagt tatgggtgga gcgcatacta cgcgagctgg 240
 gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt 300
 ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg 360
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<210> 507
 <211> 422
 <212> DNA
 <213> Homo Sapien

<400> 507
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 acagtctctg gattctccct cagcaactac gacctgaact gggcccgcca ggctccaggg 180
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaactgg 240
 gcaaaaaggcc gggtcaccat ctccaaaacc tcgaccacgg tggatctcaa gatcgccagt 300
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360
 ggtccgtgct tgcgcattct gggcccaggc accctggtca ccgtctcctt agggcaacct 420

174

aa

422

<210> 508
 <211> 411
 <212> DNA
 <213> Homo Sapien
 <220>
 <221> misc_feature
 <222> (1)...(411)
 <223> n=A,T,C or G

<400> 508
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 aggggctgga atggatcgga atcattggtg ctctgggtga cacatactac gcgagggtggg 240
 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360
 ctggttatta taaaatctgg ggcccaggca ccctgggtcac cgtctccttg g 411

<210> 509
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 509
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 510
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 510
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5 10 15

<210> 511
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
 1 5 10 15

175

<210> 512
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 512
 Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
 1 5 10 15

<210> 513
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 513
 Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
 1 5 10 15

<210> 514
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 514
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 515
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 515
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
 1 5 10 15

<210> 516
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 516
 Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln

176

1 5 10 15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1 5 10 15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1 5 10 15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1 5 10 15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 520
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
1 5 10 15
Glu Ala Arg Arg His Tyr Asp Glu Gly
20 25

<210> 521
<211> 21
<212> PRT
<213> Artificial Sequence

177

<220>

<223> Made in a lab

<400> 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

<210> 522

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

<210> 523

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<220>

<221> VARIANT

<222> (1)...(254)

<223> Xaa = any amino acid

<400> 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20					25					30		
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35				40					45				
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln
	50				55					60					
Trp	Val	Leu	Ser	Ala	Thr	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly
65				70					75					80	
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met
			85					90						95	
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu
			100					105					110		
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu
		115				120					125				
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala
	130				135						140				
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg
145					150					155					160

178

Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524
 <211> 765
 <212> DNA
 <213> Homo sapien

<400> 524
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 tcgcagccct ggcaggcggc actggtcatg gaaaacgaat tggtctgctc gggcgctcctg 180
 gtgcattccg agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300
 ctctccgtac ggcaccacaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 420
 tgcctaccg cggggaactc ttgcctcgtt tctggctggg gtctgctggc gaacggcaga 480
 atgcctaccg tgctgcagtg cgtgaacgtg tcggtggtgt ctgaggaggt ctgcagtaag 540
 ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 600
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcott 660
 gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc cagggtgtcta caccaacctc 720
 tgcaaattca ctgagtggat agagaaaacc gtccaggcca gttaa 765

<210> 525
 <211> 254
 <212> PRT
 <213> Homo sapien

<400> 525
 Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
 1 5 10 15
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
 20 25 30
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
 35 40 45
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60
 Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg

179

145		150		155		160									
Met	Pro	Thr	Val	Leu	Gln	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu	Glu
		165		170		175									
Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys
		180		185		190									
Ala	Gly	Gly	Gly	Gln	Asp	Gln	Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly
		195		200		205									
Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly
		210		215		220									
Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu
225				230		235									240
Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser		
		245		250											

<210> 526

<211> 963

<212> DNA

<213> Homo sapiens

<400> 526

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aactgcatcg tggcttctcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttgacgc cattgacctg gccttatcca catccaccat gcctaagatc 240
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963

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<210> 527

<211> 320

<212> PRT

<213> Homo sapiens

<400> 527

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Pro	Gly	Leu	Glu	Lys	Ala	His	Phe	Trp	Val	Gly	Phe	Pro	Leu	Leu	Ser
		20						25				30			
Met	Tyr	Val	Val	Ala	Met	Phe	Gly	Asn	Cys	Ile	Val	Val	Phe	Ile	Val
		35					40					45			
Arg	Thr	Glu	Arg	Ser	Leu	His	Ala	Pro	Met	Tyr	Leu	Phe	Leu	Cys	Met
	50				55					60					
Leu	Ala	Ala	Ile	Asp	Leu	Ala	Leu	Ser	Thr	Ser	Thr	Met	Pro	Lys	Ile
	65			70					75					80	
Leu	Ala	Leu	Phe	Trp	Phe	Asp	Ser	Arg	Glu	Ile	Ser	Phe	Glu	Ala	Cys
		85					90						95		
Leu	Thr	Gln	Met	Phe	Phe	Ile	His	Ala	Leu	Ser	Ala	Ile	Glu	Ser	Thr
		100					105						110		

180

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
 115 120 125
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
 130 135 140
 Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
 145 150 155 160
 Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
 165 170 175
 Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
 180 185 190
 Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
 195 200 205
 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
 210 215 220
 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
 225 230 235 240
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
 245 250 255
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
 260 265 270
 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
 275 280 285
 Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
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 305 310 315 320

<210> 528
 <211> 20
 <212> DNA
 <213> Homo Sapien

<400> 528
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<210> 529
 <211> 20
 <212> DNA
 <213> Homo Sapien

<400> 529
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20

<210> 530
 <211> 1852
 <212> DNA
 <213> Homo sapiens

<400> 530
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181

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<210> 531

<211> 879

<212> DNA

<213> Homo sapiens

<400> 531

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<210> 532

<211> 292

<212> PRT

<213> Homo sapiens

<400> 532

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Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
          35              40              45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp

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182

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Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
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Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
      100      105      110
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
      115      120      125
Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
      130      135      140
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
145      150      155      160
Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
      165      170      175
Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
      180      185      190
Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
      195      200      205
Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
      210      215      220
Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
225      230      235      240
Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
      245      250      255
Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
      260      265      270
Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
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Val Ile Ile Met
290

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<400> 533
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<210> 534
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 <213> Homo sapiens

183

<400> 534

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Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
      35              40              45
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      50              55              60
Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
      65              70              75              80
Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
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Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
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Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
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Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
      130             135             140
Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
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Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr
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Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser
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Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
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Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
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<211> 6082

<212> DNA

<213> Homo sapiens

<400> 535

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185

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<212> DNA

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<210> 537

<211> 1228

<212> PRT

<213> Homo sapiens

<400> 537

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Asn Leu Cys Ser Arg Val Phe Phe Trp Trp Leu Asn Pro Leu Phe Lys
      20              25              30
Ile Gly His Lys Arg Arg Leu Glu Asp Asp Met Tyr Ser Val Leu
      35              40              45
Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
      50              55              60
Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu
      65              70              75              80
Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly
      85              90              95
Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val Ile Gln Pro Ile Phe
      100             105             110
Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser
      115             120             125
Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys
      130             135             140
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln
      145             150             155             160
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg
      165             170             175

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188

Lys	Ala	Leu	Arg	Leu	Ser	Asn	Met	Ala	Met	Gly	Lys	Thr	Thr	Thr	Gly
		180						185					190		
Gln	Ile	Val	Asn	Leu	Leu	Ser	Asn	Asp	Val	Asn	Lys	Phe	Asp	Gln	Val
		195					200					205			
Thr	Val	Phe	Leu	His	Phe	Leu	Trp	Ala	Gly	Pro	Leu	Gln	Ala	Ile	Ala
	210					215					220				
Val	Thr	Ala	Leu	Leu	Trp	Met	Glu	Ile	Gly	Ile	Ser	Cys	Leu	Ala	Gly
225					230					235					240
Met	Ala	Val	Leu	Ile	Ile	Leu	Leu	Pro	Leu	Gln	Ser	Cys	Phe	Gly	Lys
				245					250					255	
Leu	Phe	Ser	Ser	Leu	Arg	Ser	Lys	Thr	Ala	Thr	Phe	Thr	Asp	Ala	Arg
			260					265					270		
Ile	Arg	Thr	Met	Asn	Glu	Val	Ile	Thr	Gly	Ile	Arg	Ile	Ile	Lys	Met
	275						280					285			
Tyr	Ala	Trp	Glu	Lys	Ser	Phe	Ser	Asn	Leu	Ile	Thr	Asn	Leu	Arg	Lys
	290					295					300				
Lys	Glu	Ile	Ser	Lys	Ile	Leu	Arg	Ser	Ser	Cys	Leu	Arg	Gly	Met	Asn
305					310					315					320
Leu	Ala	Ser	Phe	Phe	Ser	Ala	Ser	Lys	Ile	Ile	Val	Phe	Val	Thr	Phe
				325					330					335	
Thr	Thr	Tyr	Val	Leu	Leu	Gly	Ser	Val	Ile	Thr	Ala	Ser	Arg	Val	Phe
		340						345					350		
Val	Ala	Val	Thr	Leu	Tyr	Gly	Ala	Val	Arg	Leu	Thr	Val	Thr	Leu	Phe
	355						360					365			
Phe	Pro	Ser	Ala	Ile	Glu	Arg	Val	Ser	Glu	Ala	Ile	Val	Ser	Ile	Arg
	370					375					380				
Arg	Ile	Gln	Thr	Phe	Leu	Leu	Asp	Glu	Ile	Ser	Gln	Arg	Asn	Arg	
385					390				395					400	
Gln	Leu	Pro	Ser	Asp	Gly	Lys	Lys	Met	Val	His	Val	Gln	Asp	Phe	Thr
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Ala	Phe	Trp	Asp	Lys	Ala	Ser	Glu	Thr	Pro	Thr	Leu	Gln	Gly	Leu	Ser
		420						425					430		
Phe	Thr	Val	Arg	Pro	Gly	Glu	Leu	Ala	Val	Val	Gly	Pro	Val	Gly	
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Ala	Gly	Lys	Ser	Ser	Leu	Leu	Ser	Ala	Val	Leu	Gly	Glu	Leu	Ala	Pro
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Ser	His	Gly	Leu	Val	Ser	Val	His	Gly	Arg	Ile	Ala	Tyr	Val	Ser	Gln
465					470					475					480
Gln	Pro	Trp	Val	Phe	Ser	Gly	Thr	Leu	Arg	Ser	Asn	Ile	Leu	Phe	Gly
				485					490					495	
Lys	Lys	Tyr	Glu	Lys	Glu	Arg	Tyr	Glu	Lys	Val	Ile	Lys	Ala	Cys	Ala
		500						505					510		
Leu	Lys	Lys	Asp	Leu	Gln	Leu	Leu	Glu	Asp	Gly	Asp	Leu	Thr	Val	Ile
	515						520					525			
Gly	Asp	Arg	Gly	Thr	Thr	Leu	Ser	Gly	Gly	Gln	Lys	Ala	Arg	Val	Asn
	530					535					540				
Leu	Ala	Arg	Ala	Val	Tyr	Gln	Asp	Ala	Asp	Ile	Tyr	Leu	Leu	Asp	Asp
545					550					555					560
Pro	Leu	Ser	Ala	Val	Asp	Ala	Glu	Val	Ser	Arg	His	Leu	Phe	Glu	Leu
				565					570					575	
Cys	Ile	Cys	Gln	Ile	Leu	His	Glu	Lys	Ile	Thr	Ile	Leu	Val	Thr	His
			580					585					590		
Gln	Leu	Gln	Tyr	Leu	Lys	Ala	Ala	Ser	Gln	Ile	Leu	Ile	Leu	Lys	Asp
	595						600					605			
Gly	Lys	Met	Val	Gln	Lys	Gly	Thr	Tyr	Thr	Glu	Phe	Leu	Lys	Ser	Gly
	610					615					620				
Ile	Asp	Phe	Gly	Ser	Leu	Leu	Lys	Lys	Asp	Asn	Glu	Glu	Ser	Glu	Gln
625					630					635					640

189

Pro	Pro	Val	Pro	Gly	Thr	Pro	Thr	Leu	Arg	Asn	Arg	Thr	Phe	Ser	Glu	645	650	655
Ser	Ser	Val	Trp	Ser	Gln	Gln	Ser	Ser	Arg	Pro	Ser	Leu	Lys	Asp	Gly	660	665	670
Ala	Leu	Glu	Ser	Gln	Asp	Thr	Glu	Asn	Val	Pro	Val	Thr	Leu	Ser	Glu	675	680	685
Glu	Asn	Arg	Ser	Glu	Gly	Lys	Val	Gly	Phe	Gln	Ala	Tyr	Lys	Asn	Tyr	690	695	700
Phe	Arg	Ala	Gly	Ala	His	Trp	Ile	Val	Phe	Ile	Phe	Leu	Ile	Leu	Leu	705	710	715
Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln	Asp	Trp	Trp	Leu	Ser	720	725	730
Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val	Thr	Val	Asn	Gly	Gly	735	740	745
Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp	Tyr	Leu	Gly	Ile	Tyr	750	755	760
Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly	Ile	Ala	Arg	Ser	Leu	765	770	775
Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln	Thr	Leu	His	Asn	Lys	780	785	790
Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	Phe	Phe	Asp	Arg	Asn	795	800	805
Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	Asp	Ile	Gly	His	Leu	810	815	820
Asp	Asp	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	Ile	Gln	Thr	Leu	Leu		825	830	835
Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	Val	Ile	Pro	Trp	Ile	840	845	850
Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	Ile	Phe	Leu	Arg	Arg	855	860	865
Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	Leu	Glu	Ser	Thr	Thr	870	875	880
Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	Leu	Gln	Gly	Leu	Trp	885	890	895
Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	Gln	Glu	Leu	Phe	Asp	900	905	910
Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	Leu	Phe	Leu	Thr	Thr	915	920	925
Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	Cys	Ala	Met	Phe	Val	930	935	940
Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	Lys	Thr	Leu	Asp	Ala	945	950	955
Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	Thr	Leu	Met	Gly	Met	960	965	970
Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	Glu	Asn	Met	Met	Ile	975	980	985
Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	Glu	Lys	Glu	Ala	Pro	990	995	1000
Trp	Glu	Tyr	Gln	Lys	Arg	Pro	Pro	Pro	Ala	Trp	Pro	His	Glu	Gly	Val	1005	1010	1015
Ile	Ile	Phe	Asp	Asn	Val	Asn	Phe	Met	Tyr	Ser	Pro	Gly	Gly	Pro	Leu	1020	1025	1030
Val	Leu	Lys	His	Leu	Thr	Ala	Leu	Ile	Lys	Ser	Gln	Glu	Lys	Val	Gly	1035	1040	1045
Ile	Val	Gly	Arg	Thr	Gly	Ala	Gly	Lys	Ser	Ser	Leu	Ile	Ser	Ala	Leu	1050	1055	1060
Phe	Arg	Leu	Ser	Glu	Pro	Glu	Gly	Lys	Ile	Trp	Ile	Asp	Lys	Ile	Leu	1065	1070	1075
																1080	1085	1090
																1095	1100	

190

Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile
 1105 1110 1115 1120
 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp
 1125 1130 1135
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu
 1140 1145 1150
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr
 1155 1160 1165
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu
 1170 1175 1180
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile
 1185 1190 1195 1200
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln
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 1220 1225

<210> 538

<211> 1261

<212> PRT

<213> Homo sapiens

<400> 538

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 35 40 45
 Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
 50 55 60
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr
 65 70 75 80
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr
 85 90 95
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr
 100 105 110
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
 115 120 125
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
 130 135 140
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
 145 150 155 160
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
 165 170 175
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
 180 185 190
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
 195 200 205
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
 210 215 220
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
 225 230 235 240
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
 245 250 255
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
 260 265 270
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile

[illegible]

[illegible]

193

				1205					1210				1215
Val	Leu	Leu	Gln	Asn	Lys	Glu	Ser	Leu	Phe	Tyr	Lys	Met	Val
			1220						1225				1230
Leu	Gly	Lys	Ala	Glu	Ala	Ala	Ala	Leu	Thr	Glu	Thr	Ala	Lys
		1235						1240				1245	
Trp	Gly	Phe	Thr	Met	Leu	Ala	Arg	Leu	Val	Ser	Asn	Ser	
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<210> 539
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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

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<210> 540
 <211> 9
 <212> PRT
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<220>
 <223> Made in a lab

<400> 540
 Ala Val Val Thr Ala Ser Ala Ala Leu
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<210> 541
 <211> 14
 <212> PRT
 <213> Homo sapiens

<400> 541
 Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
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<210> 542
 <211> 15
 <212> PRT
 <213> Homo sapiens

<400> 542
 Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 5 10 15

<210> 543
 <211> 12
 <212> PRT
 <213> Homo sapiens

<400> 543
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<210> 544
<211> 18
<212> PRT
<213> Homo sapiens
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<400> 544
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<210> 545
<211> 18
<212> PRT
<213> Homo sapiens
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<400> 545
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Ser Val

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<210> 546
<211> 29
<212> PRT
<213> Homo sapiens
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<400> 546
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Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
          20                      25

```

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<210> 547
<211> 58
<212> PRT
<213> Homo sapiens
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```

<400> 547
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Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
              20                      25                      30
Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
              35                      40                      45
Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
              50                      55

```

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<211> 18
<212> PRT
<213> Homo sapiens
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<400> 548
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195

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Glu Cys			

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<210> 549
<211> 18
<212> PRT
<213> Homo sapiens
```

```

<400> 549
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Gln Ala

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<210> 550
<211> 14
<212> PRT
<213> Homo sapiens
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<400> 550
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<210> 551
<211> 11
<212> PRT
<213> Artificial Sequence
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<220>
<223> Made in a lab

<400> 551
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5 10

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<210> 552
<211> 2577
<212> DNA
<213> Homo sapiens
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400> 552						
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196

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agttaggaat taaacccagt attgtgtgaa tctaaagcct aacttttttc tctttatcac 2520
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```

<210> 553

<211> 58

<212> PRT

<213> Homo sapiens

<400> 553

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Ser Ile Cys Asn Met Thr Cys Ala Ser Val Phe Phe Cys Asp Gln Lys
              5              10              15
Phe Leu Thr Phe Ser Phe Leu Ser Met Val Glu Pro Pro Arg Ala Gly
              20              25              30
Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
              35              40              45
Glu Pro His His Thr Gly Gly Gly Glu His
              50              55

```

<210> 554

<211> 59

<212> PRT

<213> Homo sapiens

<400> 554

```

Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
              5              10              15
Cys Ala Ala Glu Ala Ser Thr Lys Pro Tyr Phe Tyr Thr Cys Leu Val
              20              25              30
Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
              35              40              45
Glu Ile Leu Arg Phe Leu Phe Asn Gly Phe Leu
              50              55

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197

<210> 555
 <211> 71
 <212> PRT
 <213> Homo sapiens

<400> 555
 Leu Gly Arg Phe Ser Leu Ser Cys Lys Ser Gly His Ser Arg Gly Gln
 5 10 15
 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser
 20 25 30
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp
 35 40 45
 Leu Val Ala Lys Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro
 50 55 60
 Ser Asp Pro Leu Glu Leu Leu
 65 70

<210> 556
 <211> 81
 <212> PRT
 <213> Homo sapiens

<400> 556
 Asn His Pro Glu Gln Gly Ser Ser Thr Pro Arg Pro Gln Thr His Thr
 5 10 15
 Ser Pro Arg Thr Ile Met Asn His Thr Thr Gln Glu Glu Val Ser Thr
 20 25 30
 Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly
 35 40 45
 Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile
 50 55 60
 Arg Asn Ser Leu Glu His Glu Pro Cys Cys Glu Leu Pro Ile Arg Arg
 65 70 75 80
 Ile

<210> 557
 <211> 54
 <212> PRT
 <213> Homo sapiens

<400> 557
 Ser Leu Ser Ala Thr Pro Leu Thr Leu Trp Asn Ser Ser Asp Pro Leu
 5 10 15
 Glu Gln Ala Tyr Leu Ile Ser Ala Arg Glu Lys Thr Asn Asn Gly Leu
 20 25 30
 Lys Gly Ser Leu Thr Met Lys Val Ser Ala Asn Ser Trp Leu Arg Cys
 35 40 45
 Gly Phe His Ile Arg Phe
 50

<210> 558
 <211> 77
 <212> PRT
 <213> Homo sapiens

198

<220>

<221> VARIANT

<222> (1)...(77)

<223> Xaa = Any amino acid

<400> 558

```

Asn Asp Arg Asp Arg Asn Ser Asn Lys Val Ile Xaa Lys Ala Asn Leu
              5              10              15
Ile Tyr Phe Thr Asn Leu Thr Ser Cys Leu Ser Val Gln Asn Gln Thr
              20              25              30
Phe Thr Cys Thr Lys Arg His Lys His Leu Gln Cys Ser Ser Val His
              35              40              45
Leu Cys Lys Ile Pro Pro Arg Leu Lys Gly Arg Asp Lys Lys Lys Lys
              50              55              60
Pro Ser Tyr Leu Ser Gly Val Leu His Ser Arg Ser Tyr
              65              70              75

```

<210> 559

<211> 50

<212> PRT

<213> Homo sapiens

<400> 559

```

Thr Leu Pro Pro Leu Arg Ser Val Ile Thr Leu Glu Thr His Trp Ser
              5              10              15
Thr Asn Pro Val Val Asn Cys Leu Ser Glu Gly Ser Arg Leu Cys Ala
              20              25              30
Ser Tyr Glu Asn Leu Met Pro Asp Asp Leu Ser Leu Ser His Phe Ala
              35              40              45
Pro Arg
              50

```

<210> 560

<211> 56

<212> PRT

<213> Homo sapiens

<400> 560

```

Ile Gly Ser Leu Lys Gly Pro Thr Thr Ala Gly Ser His Cys Ser Gly
              5              10              15
Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr
              20              25              30
Lys Gly Ala Ser Gln Tyr Arg Ser Gly Ser Lys Glu Glu Glu Thr Asn
              35              40              45
Thr Asp Leu Phe Leu Pro Pro Leu
              50              55

```

<210> 561

<211> 57

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

199

<222> (1)...(57)

<223> Xaa = Any amino acid

<400> 561

```

Val Leu His Leu Asp Gln Met Asn Asn Val Gly Ile Xaa Met Asp Lys
              5              10              15
Gly Leu Lys Ser Pro Glu Ile Lys Asn Pro Ala Pro Thr Gly Thr Ser
              20              25              30
Asn Leu Ser Cys Phe Leu Ser Xaa Phe Trp Leu Met Gln Gly Thr Asn
              35              40              45
Ser Leu Pro Arg Glu Asn Tyr Leu Asn
              50              55

```

<210> 562

<211> 59

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> (1)...(59)

<223> Xaa = Any amino acid

<400> 562

```

Asp Leu Tyr Pro Xaa Arg Ser Gln His Cys Ser Phe Asp Pro Ser Val
              5              10              15
Ala Pro Met His Gly Ile Lys Asn Ser Ile Thr Ser Leu Ile Phe Leu
              20              25              30
Ile Ser Tyr Leu Xaa Leu Glu Met Ser Ser Leu Ser Glu Ser Leu Val
              35              40              45
Leu Ser Ser Gly Asp Tyr Val Leu Asp Thr Pro
              50              55

```

<210> 563

<211> 79

<212> PRT

<213> Homo sapiens

<400> 563

```

Cys Phe Leu Phe Pro Tyr Leu Trp Leu Tyr Ala Gln Pro Leu Phe Pro
              5              10              15
Lys Gln Gln Pro Pro Ala Leu Ala Pro Gly His Pro Asp Phe Ile His
              20              25              30
Thr Gln Asn Glu Gln Ile Asp Pro Ser Pro His Ile Gln Asn Leu Met
              35              40              45
Trp Asn Pro His Leu Ser Gln Glu Leu Ala Glu Thr Phe Met Val Arg
              50              55              60
Asp Pro Leu Arg Pro Leu Leu Val Phe Ser Leu Ala Asp Ile Arg
              65              70              75

```

<210> 564

<211> 64

<212> PRT

<213> Homo sapiens

<400> 564

200

Ala Cys Ser Lys Gly Ser Glu Glu Phe Gln Arg Val Arg Gly Val Ala
 5 10 15
 Glu Arg Asp Gln Cys Leu Phe Leu Leu Leu Cys Tyr Gln Ile Tyr Thr
 20 25 30
 Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser
 35 40 45
 His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro
 50 55 60

<210> 565

<211> 57

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> (1)...(57)

<223> Xaa = Any amino acid

<400> 565

Leu Tyr Tyr Cys Ser Tyr Leu Cys His Phe Arg Thr Ala Leu Ile Leu
 5 10 15
 Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln
 20 25 30
 Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu
 35 40 45
 Tyr Ala Val Ser Ser Xaa His Asn Val
 50 55

<210> 566

<211> 55

<212> PRT

<213> Homo sapiens

<400> 566

Ile Leu Leu Glu Phe Phe Arg Asn Gln Arg Gly Ser Leu Asn Pro Arg
 5 10 15
 Lys Thr Val Pro Phe Ile Lys Ser Glu Gly Gly Glu Lys Lys Gly His
 20 25 30
 Cys Asn His Ser Val Val Ser Ile Asp Ser Ala Ala Ala Leu Leu Pro
 35 40 45
 Leu Lys Leu Val Leu Leu Pro
 50 55

<210> 567

<211> 51

<212> PRT

<213> Homo sapiens

<400> 567

Tyr Ser Asp Phe Asp Val Phe Cys Ser His Thr Tyr Gly Tyr Met Leu
 5 10 15
 Ser His Cys Ser Gln Ser Ser Ser Pro Leu Leu Trp Pro Leu Gly Ile
 20 25 30
 Leu Thr Leu Ser Thr His Lys Met Ser Lys Leu Thr Leu Pro Pro Ile

201

35
Phe Arg Thr
50

40

45

<210> 568
<211> 75
<212> PRT
<213> Homo sapiens

<400> 568
Lys Val Gly Glu Tyr Ile Leu Gln Ser Leu Leu Arg Ile Arg Lys Ile
5 10 15
Tyr Val Ala Phe Asn Ser Val Pro Ser Thr Cys Leu Leu Ala Ser Leu
20 25 30
Thr Glu Thr Pro Val Thr Thr Ile Leu Thr Ile Ile Ile Asn Leu Thr
35 40 45
Cys Phe Gln His Ala Glu Ser Tyr Leu Phe Tyr Pro Leu Ala Asp
50 55 60
Phe Leu Leu Gln His Ile Ser Leu Gly Lys Leu
65 70 75

<210> 569
<211> 4809
<212> DNA
<213> Homo sapiens

<400> 569
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aaatacacac tgtactaaga atctacacac cgaaagacaa aaacaagaca aatttgagtg 540
ctacagggtgt cacgcttggt atcacacatg tgccctgtgta ttcctctagg tggttaccag 600
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<210> 570

<211> 951

<212> DNA

<213> Homo sapiens

<400> 570

203

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ccatttttagt actatgggtg agtacatgga attgaagtct ggcttaaadc ttcagaaagt 180
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<210> 571

<211> 819

<212> DNA

<213> Homo sapiens

<400> 571

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cctgggaggg ctgaggagga gaatcgcttg aaccgggag gcagagggtg cagtgaaccg 720
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aaataaacia acaaaciaac aaaacagaga gattttgct 819

```

<210> 572

<211> 203

<212> DNA

<213> Homo sapiens

<400> 572

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atcaggtctc atgagaactc atg 203

```

<210> 573

<211> 132

<212> PRT

<213> Homo sapiens

<400> 573

```

Met Val Glu Gly Glu Glu Ala Arg His Val Leu His Gly Gly Arg
          5              10              15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg

```

204

```

      20      25      30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
      35      40      45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
      50      55      60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
      65      70      75      80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
      85      90      95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
      100      105      110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
      115      120      125
Leu Leu Asn Tyr
      130

```

<210> 574
 <211> 62
 <212> PRT
 <213> Homo sapiens

```

<400> 574
Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
      5      10      15
His Gly Gly Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
      20      25      30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
      35      40      45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
      50      55      60

```

<210> 575
 <211> 76
 <212> PRT
 <213> Homo sapiens

```

<400> 575
Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
      5      10      15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
      20      25      30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
      35      40      45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
      50      55      60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
      65      70      75

```

<210> 576
 <211> 68
 <212> PRT
 <213> Homo sapiens

<220>
 <221> VARIANT

205

<222> (1)...(68)

<223> Xaa = Any Amino Acid

<400> 576

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Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr
              5              10              15
Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
              20              25              30
Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
              35              40              45
Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
              50              55              60
Pro Gly Tyr Ser
65

```

<210> 577

<211> 57

<212> PRT

<213> Homo sapiens

<400> 577

```

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
              5              10              15
Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
              20              25              30
Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
              35              40              45
Arg Leu Ala Pro Pro Ala Asp Thr Pro
              50              55

```

<210> 578

<211> 51

<212> PRT

<213> Homo sapiens

<400> 578

```

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
              5              10              15
His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr
              20              25              30
Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr
              35              40              45
Gln Pro His
50

```

<210> 579

<211> 56

<212> PRT

<213> Homo sapiens

<400> 579

```

Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
              5              10              15
Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
              20              25              30
Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
              35              40              45
Ile Ala Lys Val Tyr Gln Pro His

```

206

50

55

<210> 580

<211> 67

<212> PRT

<213> Homo sapiens

<400> 580

```

Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
              5              10              15
Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
              20              25              30
Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
              35              40              45
His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
              50              55              60
Phe Ile His
              65

```

<210> 581

<211> 77

<212> PRT

<213> Homo sapiens

<400> 581

```

Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
              5              10              15
Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
              20              25              30
Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
              35              40              45
Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
              50              55              60
Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
              65              70              75

```

<210> 582

<211> 51

<212> PRT

<213> Homo sapiens

<400> 582

```

Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
              5              10              15
Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
              20              25              30
Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
              35              40              45
Leu Gly Val
              50

```

<210> 583

<211> 60

<212> PRT

<213> Homo sapiens

<400> 583

```

Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg

```

207

```

          5          10          15
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          20          25          30
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          35          40          45
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          50          55          60

```

<210> 584

<211> 76

<212> PRT

<213> Homo sapiens

<400> 584

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

<210> 585

<211> 50

<212> PRT

<213> Homo sapiens

<400> 585

```

Met Val Tyr Arg Phe Gly Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu
          5          10          15
Ala Ser Leu Gly Ser Ser Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp
          20          25          30
Arg Gln Ala Asp Pro Ser Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu
          35          40          45
Leu Phe
          50

```

<210> 586

<211> 60

<212> PRT

<213> Homo sapiens

<400> 586

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

<210> 587

<211> 1408

<212> DNA

<213> Homo sapiens

<400> 587

```

ctggacactt tgcgagggct tttgctggct gctgctgctg cccgtcatgc tactcatcgt 60
agcccgcccc gtgaagctcg ctgctttccc tacctcctta agtgactgcc aaacgcccac 120
cggctggaat tgctctgggt atgatgacag agaaaatgat ctcttctctt gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa 300
tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tgggtgcaga 360
aggatcatgt gccacagatg caggatcagg atctggagat ggagtccatg aaggctctgg 420
agaaactagt caaaaggaga catccacctg tgatatattg cagtttggtg cagaatgtga 480
cgaagatgcc gaggatgtct ggtgtgtgtg taatatgtac tgttctcaaa ccaacttcaa 540
tccccctctg cttctgatg ggaaatctta tgataatgca tgccaaatca aagaagcatc 600
gtgtcagaaa caggagaaaa ttgaagtcac gtctttgggt cgatgtcaag ataacacaac 660
tacaactact aagtctgaag atgggcatta tgcaagaaca gattatgcag agaatgctaa 720
caaattagaa gaaagtgccg gagaacacca cataccttgt ccggaacatt acaatggcct 780
ctgcatgcat ggaagtgtg agcattctat caatatgcag gagccatctt gcaggtgtga 840
tgctggttat actggacaac actgtgaaaa aaaggactac agtgttctat acgttggttc 900
cggctcctgta cgatttcagt atgtcttaac cgacagctgtg attggaacaa ttcagattgc 960
tgtcatctgt gtggtggtcc tctgcatcac aaggaaatgc cccagaagca acagaattca 1020
cagacagaag caaaatacag ggcactacag ttcagacaat acaacaagag cgtccacgag 1080
gttaacttaa agggagcatg tttcacagtg gctggactac cgagagcttg gactacacaa 1140
tacagtatta tagacaaaag aataagacaa gagatctaca catgttgcct tgcatttgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatattt gattatgtat ggatatattt 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320
caatawagtt ttttctttcc catgtatttg ttatatataa taaatactca gtgatgagaa 1380
aaaaaaaaa aaaaaaaaaa rwmgaccc 1408

```

<210> 588

<211> 81

<212> PRT

<213> Homo sapiens

<400> 588

```

Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
                    5                      10                      15
Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
                    20                      25                      30
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
                    35                      40                      45
Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
                    50                      55                      60
Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
                    65                      70                      75                      80
Ile

```

<210> 589

<211> 157

<212> PRT

<213> Homo sapiens

<400> 589

```

Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
                    5                      10                      15
Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
                    20                      25                      30
Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu

```

209

```

      35      40      45
Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
  50      55      60
Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
  65      70      75      80
Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
      85      90      95
Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
      100      105      110
Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
      115      120      125
Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
      130      135      140
Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
      145      150      155

```

<210> 590

<211> 347

<212> PRT

<213> Homo sapiens

<400> 590

```

Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
      5      10      15
Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
      20      25      30
Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
      35      40      45
Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
      50      55      60
Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
      65      70      75      80
Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
      85      90      95
Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
      100      105      110
Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
      115      120      125
Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
      130      135      140
Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
      145      150      155      160
Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
      165      170      175
Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
      180      185      190
Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr
      195      200      205
Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu Asn Ala
      210      215      220
Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys Pro Glu
      225      230      235      240
His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser Ile Asn
      245      250      255
Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly Gln His
      260      265      270
Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly Pro Val

```


210

275	280	285
Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile Gln Ile		
290	295	300
Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys Pro Arg		
305	310	315
Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr Ser Ser		
	325	330
		335
Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile		
340	345	

<210> 591

<211> 565

<212> DNA

<213> Homo sapien

<400> 591

actaaagcaa atgaacaagc tgacttgcta gtatcatctg cattcattga agcacaagaa	60
cttcatgcct tgactcatgt aaatgcaata ggattaaaaa ataaatttga tatcacatgg	120
aaacagacaa aaaatattgt acaacattgc acccagtgtc agattctaca cctggccact	180
caggaagcaa gagttaatcc cagaggtcta tgcctaata tggtatggca aatggatgtc	240
atgcacgtac cttcatttgg aaaattgtca tttgtccatg tgacagttga tacttattca	300
catttcatat gggcaacctg ccagacagga gaaagtactt cccatgttaa aagacattta	360
ttatcttgtt ttccctgtcat gggagttcca gaaaaagtta aaacagacaa tgggccagg	420
tactgtagta aagcatttca aaaattotta aatcagtgga aaattacaca tacaatagga	480
attctctata attcccaagg acaggccata attgaaggaa ctaatagaac actcaaagct	540
caattgggta aacaaaaaaa aaaaa	565

<210> 592

<211> 188

<212> PRT

<213> Homo sapien

<400> 592

Thr Lys Ala Asn Glu Gln Ala Asp Leu Leu Val Ser Ser Ala Phe Ile	
1	15
Glu Ala Gln Glu Leu His Ala Leu Thr His Val Asn Ala Ile Gly Leu	
20	30
Lys Asn Lys Phe Asp Ile Thr Trp Lys Gln Thr Lys Asn Ile Val Gln	
35	45
His Cys Thr Gln Cys Gln Ile Leu His Leu Ala Thr Gln Glu Ala Arg	
50	60
Val Asn Pro Arg Gly Leu Cys Pro Asn Val Leu Trp Gln Met Asp Val	
65	80
Met His Val Pro Ser Phe Gly Lys Leu Ser Phe Val His Val Thr Val	
85	95
Asp Thr Tyr Ser His Phe Ile Trp Ala Thr Cys Gln Thr Gly Glu Ser	
100	110
Thr Ser His Val Lys Arg His Leu Ser Cys Phe Pro Val Met Gly	
115	125
Val Pro Glu Lys Val Lys Thr Asp Asn Gly Pro Gly Tyr Cys Ser Lys	
130	140
Ala Phe Gln Lys Phe Leu Asn Gln Trp Lys Ile Thr His Thr Ile Gly	
145	160
Ile Leu Tyr Asn Ser Gln Gly Gln Ala Ile Ile Glu Gly Thr Asn Arg	
165	175
Thr Leu Lys Ala Gln Leu Val Lys Gln Lys Lys Lys	
180	185

211

<210> 593
 <211> 271
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(271)
 <223> n = A,T,C or G

<400> 593
 actttatgtt cnagtgcana aancncctg gattgccacc ntactctcag ggctgtgant 60
 tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggg 120
 gtccctagct ggggtctata catgncnggg naagggcngc tgagtnccat nagcaaagga 180
 nctagnatnt gcgggggtgc ggccctgggc taccctttna agcatccntn gatccactcc 240
 angaancng gggtagnacg gtttnccaac a 271

<210> 594
 <211> 376
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(376)
 <223> n = A,T,C or G

<400> 594
 cctttggggg nggggggaac ctttaccatt gtnccccttt atttcatttg gttnggggttc 60
 gcgccctcnn gggccaacaa agttatcgtn nttgaagaga anattttttt ggnttngncc 120
 cgattaagcg ncaaagtgtg agcaaaaangc cgtgccactt gtggcgtagc tncgtcgggt 180
 cgattcgacg acaaggcgtn gcgcgtanc gttagtctcn aatngaccn gtggcatgag 240
 cccacgangg nttcgtgtcg tcacatggnc tctagacata acgcncncn ttttttncag 300
 agggggntgc cgccttagg gaggnagggg tggggacact agccaancca nantctnacc 360
 ccattgaaga aaaggn 376

<210> 595
 <211> 242
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(242)
 <223> n = A,T,C or G

<400> 595
 agnctgctgn tcgtnccctn tatgtggctt catnntgagg acaanagtng cactgaggct 60
 tgngnatgcc aggcaaggnc aagctggctc aaaaagcatc caccacctc tgnaangggg 120
 atgccangag cangtgcacc agtcccaact angagnccn ggcagtntac atcttcttcc 180
 acccctnaaa ntttnggcta caangnccat ttttctttt ctcttaaggg ncnctnggct 240
 tc 242

<210> 596
 <211> 535
 <212> DNA
 <213> Homo sapien

212

<220>

<221> misc_feature

<222> (1)...(535)

<223> n = A,T,C or G

<400> 596

accagttgga tactgctaaa nagatattta tgcagcctca tatgttaagt cgtatatattt	60
gaaagctttt taaatttttt ctttaagaag atttttagatg cttatcactg agtaccagag	120
ggatgtaggc tgatgccctt atcaacaaag tcagggactg tggcacacaa ggattgacta	180
ctgcagacac ggccacaatg ctacctctag agggcctgaa tccccctgcc ctctctgggtg	240
gggagaaggg ctggcagagc cattagcatg ggctccggcc aatcctggcc actttgacac	300
tcctggtgct gaccaggggt cctggaggaa gggatgaggt gggcagtaga gatgctcagg	360
gcagtggccc ctttccatcc aacttggaac tatttcagta ttttaccacc aattcagcca	420
ttcccttggtg cgtggtctga acatcagccc tgcctcagggt ctcatgtttcc cctttgtaaa	480
gggaaagctc tggattcagg gattgatgaa gaggtcatca tggctcttgag aattc	535

<210> 597

<211> 257

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(257)

<223> n = A,T,C or G

<400> 597

tttcnatacc caaaantacc ccatattang accanacatt tgcctnggaa aaattaccat	60
tntntaactt ttgggccacc tgagannaaa tgggtgtaat ncatgataag atggancagn	120
atttctctta agatnngatn agaccccggtt tttcaoggaa catatccaag nacccaatag	180
gnaacaagcc acgggnggag tcacaaacat atattcttta ctctcataat ccgtnnnaca	240
naactnttgn acttgac	257

<210> 598

<211> 222

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(222)

<223> n = A,T,C or G

<400> 598

nttggntacc gtcnaaactt ncttgggtac ccgagctcgg atccactagt ccagtgtggt	60
ggaattccat tgtgttgggc tataagctgt aatagtggag nctgtctngg ttcattgcan	120
nagnccctcc gcanncacnc ttgnnacaac ctgtgagnag gcnataaatt attcacataa	180
tcatcactgc atgaanctga ctcaaacgca tccacntaca cc	222

<210> 599

<211> 238

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(238)

213

<223> n = A,T,C or G

<400> 599

gcatgacatc	ancgatgtnt	ttggnnacct	ganattngct	aaaactngng	natgccgggn	60
atgnaggttt	ggtantgatc	tatgcactca	catctcatgg	ggacgtttca	tgtggagtgn	120
tcgacaangt	tgctgnannc	gagaagtgat	gatctcagtt	gaaaggggtca	tgtgaataca	180
cnttacactt	gaaaaagaag	cacattggga	atatcacgaa	acgnccacca	acatcctg	238

<210> 600

<211> 232

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(232)

<223> n = A,T,C or G

<400> 600

cgaactat	agactaccta	ggaaaattat	tttagtatca	gaagaatatc	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatgttag	tttgtcttcc	gccatttcta	120
cagaaagctg	caatttcagg	ttttcaacct	aataggtgat	atttaanaaa	aaaaaaaaagc	180
aatcgcaaat	agccccactg	cttttacaaa	tcattttttc	cccaacacaa	tg	232

<210> 601

<211> 547

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(547)

<223> n = A,T,C or G

<400> 601

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcga	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tgcagctttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatttag	ctctgatgag	tactacacc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagttag	taactcaaaa	cgagtgcac	tnggaagtat	cgcagccgtt	300
nectgatnaa	attcccagct	tgctngcttg	ctnagccggg	gggcggtnaa	aaaaacatct	360
gcagcccngg	ggnaaaaacc	ttcgattgt	tcttacgtgt	ttacgttatt	ttatttccct	420
nnagcaaggc	nggganttgg	ggactcgaaa	tggtacagtt	gggctgggga	tcgcccttgt	480
tacataaaag	ncgtccagaa	gagggacggt	tacaggcngg	ganctccaaa	ggtcagtccc	540
tgccatt						547

<210> 602

<211> 826

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(826)

<223> n = A,T,C or G

<400> 602

cggggggnnt	tacgtctctc	tgacgctttt	tattgtacca	gggcgatccc	agcccaactg	60
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214

taccattcga	gtccctactc	ctgccttgct	ctagggaaat	aaaataacgt	aaacacgtaa	120
gaacaatgcg	aaagcgTTTT	cttccttagg	ctgcagattg	tcttcttcac	cgccctgct	180
tagctagcta	gctagctggg	aatttaatcc	agaaacggct	tgcgatacct	cctagatgca	240
ctcgTTTTga	gttacaaact	ccgcggatta	catgtctttt	taaaaaagtt	tagactacac	300
tagggaaaaat	tatttttagta	tcagaagaat	atcagggggt	gtagtactca	tcagagctna	360
atgagagcgc	tttaaaaaatg	ttagtttgct	ttccgccatt	tctacagaaa	gctgcaattt	420
caggTTTTca	ncctaatagg	tgatatntaa	gaaaaaaaaa	acaatcgcan	atagcccaact	480
gctttttacaa	atcatttttct	tcttctagggt	atagcctgtc	aggtggccta	atgtattttt	540
gacatctcta	ggaatttttaa	tagaccagaa	atgggtgccca	gagatatgcc	tgactaatac	600
ttaagtgggg	atttatgtat	ttctcaanca	agtgattaaa	gcaaaactag	gcacgaatga	660
aatcaagatc	tttaggccag	aatcatgaa	nanttttana	attattttan	gaatctgtgg	720
cttctcttct	taaaatngaa	aaaaaaattg	tttaaaccca	naaggtctga	ataccaagc	780
nccctgaacn	anagaacaan	gccggagcac	cccctcccaa	atcccc		826

<210> 603
 <211> 817
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(817)
 <223> n = A,T,C or G

<400> 603	
nnangacttt	tgtggtntta
agtcctaaaa	taattctaaa
tcgtgcctag	ttttgcttta
agtgccagga	tatctctggc
aattacatta	ggccacctga
gtggggctat	ttgcgattgc
tgaaattgca	gctttctgta
atttagctct	gatgagtact
gtgtagtcta	aaacttttta
tgcatctagg	aggatatgca
agcaggggcg	ggnaaanaag
tacgtgttta	cgttatttta
ttgggggtgg	ggatccccctg
agggtcgtcc	tgcatttana
tacaattntt	ttttctattt
actcatcatg	actttcttgc
atcacttgct	tgagaaatac
acccatttct	ggttctatta
ctagaagaga	aaaaatgatt
tcttaaatat	cacctattag
gaaatggcgg	aagacaaact
acaccctga	tattctctg
taatccgcgg	agtttgtaac
agcggtttct	ggattaaatt
cctaggggaag	aaaacctttc
caaggcngaa	ttgggactcg
ngtcanaaag	anggtacagg
ctcggaattt	tggtgcc
aaagccacag	60
ttgatttcaa	120
acttaagatt	180
agatgtcaaa	240
tgtaaaagca	300
gttgaaaacc	360
aagcgctctc	420
aattttccta	480
tcaaaacgag	540
ttgcttgctt	600
gcattgttct	660
aatggttcag	720
cggaacncca	780
	817

<210> 604
 <211> 694
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 604	
cttttcaaat	catttttinct
gacatctcta	ngaatttttaa
cttaagtggg	gatttatgta
aaatcaagat	cttttaggca
tggtctttct	ttcatagaaa
agccaaagca	acactganca
aattatacta	ccagggtgta
tancctgtca	ggtggcctaa
agagatatgc	ctgcactaat
agcaaaacta	ggcagcattg
agaattattt	taggactctg
aaccacaaaa	ggtcctgaat
caacacacta	ccngaattca
cagcattcta	ttggcataaa
atagacacca	420

215

```

agaccaatgg ancagaataa agaacccccac aaataaatcc atatatntac cgccanctga      480
ttatcaataa cnaacaccaa gaacatatnt taagggaacnt nctattcaat aantagtgct      540
ggnaaaaaact gggaaatcca tatgcagaaa naatgaaact agaccctat ccctcaccat      600
acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact      660
atnaaancta ctattaagaa aacagatcnc nccc                                694

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<210> 605

<211> 678

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(678)

<223> n = A,T,C or G

<400> 605

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taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt      60
actcatcana gctaaatgag agcgctttaa aaatgtagt ttgtcttccg ccatttctac      120
agaaagctgc aatttcaggt tttcaaccta atagggtgata ttttaagaaa aaaaaaagca      180
atcgcaaata gccccactgc ttttacaat catTTTTTct cttctaggta tagcctgtca      240
ggtggcctaa tgtaattttt gacatctcta ggaattttaa tagaaccaga aatgggtgcc      300
agagatatgc ctgcactaat cttaagtggg gatTTTatgta tttctcaagc aagtgattaa      360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt      420
anaattattt taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata      480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga      540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct      600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat      660
cctatattta cngcccnc                                678

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<210> 606

<211> 263

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(263)

<223> n = A,T,C or G

<400> 606

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gtggggctcng cancagccaa ctcagcttcc tttcgggctt tgtagcaga cggatcatcc      60
tctagtccac tgtgntcaaa ttccattgtg tgggggccnc tcgcctcggc canagatctg      120
agtgancana cntgtcccca ctgaggtgcc ccacagcngn ttgtnttcag cangggctna      180
caactcgacc ggcagcgnan ggctggcaga antgngcgcc tnnctcattc ctacgcngtn      240
ngccgcagga aggangacag gcc                                263

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<210> 607

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 607

ccatgtgggt cccggttgct tt

22

216

<210> 608
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 608
gataggggtg ctcaggggtt gg

22

<210> 609
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 609
gctggacagg gggcaaaagc tggggcagtg aaccatgtgc

40

<210> 610
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 610
ccttgtccag atagcccagt agctgac

27

<210> 611
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 611
gatagagaaa accgtccagg ccagtattgt gggaggctgg gagtgc

46

<210> 612
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 612
gcacatgggt cactgcccc gcttttgccc cctgtccagc

40

<210> 613
<211> 38
<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 613

gccgctcgag ttagaattcg gggttggcca cgatggtg

38

<210> 614

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 614

cggcgggcat atgcatcacc atcaccatca catcataaac ggcgaggact gca

53

<210> 615

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 615

gcactcccag cctcaccacaa tactggcctg gacggttttc tctatc

46

<210> 616

<211> 1350

<212> DNA

<213> Homo sapien

<400> 616

atgcatcacc atcaccatca catcataaac ggcgaggact gcagcccgca ctgcagccc	60
tggcaggcgg cactggatcat ggaaaacgaa ttgttctgct cgggcgtcct ggtgcatccg	120
cagtggtggtc tgtcagccgc acactgtttc cagaactcct acaccatcgg gctgggcctg	180
cacagtcttg aggcgacca agagccaggg agccagatgg tggaggccag cctctccgta	240
cggcaccag agtacaacag acccttgctc gctaaccgacc tcatgctcat caagttggac	300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc	360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc	420
gtgctgcagt gcgtgaacgt gtcgggtggtg tctgaggagg tctgcagtaa gctctatgac	480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc	540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc	600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc	660
actgagtgga tagagaaaac cgtccaggcc agtattgtgg gaggctggga gtgcgagaag	720
cattcccaac cctggcagggt gcttgtggcc tctcgtggca gggcagctctg cggcgggtgt	780
ctggtgcaac cccagtgggt cctcacagct gccactgca tcaggaacaa aagcgtgatc	840
ttgctgggtc ggcacagcct gtttcatcct gaagacacag gccaggtatt tcaggtcagc	900
cacagcttcc cacaccgct ctacgatatg agcctcctga agaatcgatt cctcaggcca	960
ggtgatgact ccagccacga cctcatgctg ctccgcctgt cagagcctgc cgagctcacg	1020
gatgctgtga aggtcatgga cctgcccacc caggagccag cactggggac cacctgctac	1080
gcctcaggct ggggcagcat tgaaccagag gagttcttga ccccaaagaa acttcagtgt	1140
gtggacctcc atgttatttc caatgacgtg tgtgcgcaag ttcacctca gaaggtgacc	1200
aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa gctggggcag tgaacctgt	1260
gccctgcccg aaaggccttc cctgtacacc aagggtggtgc attaccggaa gtggatcaag	1320

218

gacaccatcg tggccaaccc cgaattctaa

1350

<210> 617

<211> 449

<212> PRT

<213> Homo sapien

<400> 617

Met	His	His	His	His	His	His	Ile	Ile	Asn	Gly	Glu	Asp	Cys	Ser	Pro
1				5					10					15	
His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu	Val	Met	Glu	Asn	Glu	Leu	Phe
			20					25					30		
Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Ser	Ala	Ala	His
		35					40					45			
Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu	Glu
	50					55					60				
Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val	Glu	Ala	Ser	Leu	Ser	Val
65					70					75					80
Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu
				85					90					95	
Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile
			100					105					110		
Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser
	115					120						125			
Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys
	130					135					140				
Val	Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp
145					150					155					160
Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Asp	Gln
				165					170					175	
Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly
			180					185					190		
Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val
	195						200					205			
Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile
	210					215					220				
Glu	Lys	Thr	Val	Gln	Ala	Ser	Ile	Val	Gly	Gly	Trp	Glu	Cys	Glu	Lys
225					230					235					240
His	Ser	Gln	Pro	Trp	Gln	Val	Leu	Val	Ala	Ser	Arg	Gly	Arg	Ala	Val
				245					250					255	
Cys	Gly	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Thr	Ala	Ala	His
			260					265					270		
Cys	Ile	Arg	Asn	Lys	Ser	Val	Ile	Leu	Leu	Gly	Arg	His	Ser	Leu	Phe
		275					280					285			
His	Pro	Glu	Asp	Thr	Gly	Gln	Val	Phe	Gln	Val	Ser	His	Ser	Phe	Pro
	290					295					300				
His	Pro	Leu	Tyr	Asp	Met	Ser	Leu	Leu	Lys	Asn	Arg	Phe	Leu	Arg	Pro
305					310					315					320
Gly	Asp	Asp	Ser	Ser	His	Asp	Leu	Met	Leu	Leu	Arg	Leu	Ser	Glu	Pro
				325					330					335	
Ala	Glu	Leu	Thr	Asp	Ala	Val	Lys	Val	Met	Asp	Leu	Pro	Thr	Gln	Glu
			340					345					350		
Pro	Ala	Leu	Gly	Thr	Thr	Cys	Tyr	Ala	Ser	Gly	Trp	Gly	Ser	Ile	Glu
		355					360					365			
Pro	Glu	Glu	Phe	Leu	Thr	Pro	Lys	Lys	Leu	Gln	Cys	Val	Asp	Leu	His
	370					375					380				
Val	Ile	Ser	Asn	Asp	Val	Cys	Ala	Gln	Val	His	Pro	Gln	Lys	Val	Thr
385					390					395					400

219

Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Trp Gly
 405 410 415
 Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val
 420 425 430
 Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro Glu
 435 440 445
 Phe

<210> 618
 <211> 385
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(385)
 <223> n = A,T,C or G

<400> 618
 ctgtgctgag aaccaaagc tatgancact gcttttccaa atgtccataa naccaacatt 60
 tttatcacta ccaccatcac ctgggagctc nttagaaagc tagtctcccg ggcaccaccc 120
 tggcctactg aacctaattgt gcatttaaca agattnacgt ngaaatctgc aaagcacagg 180
 ggcngataac agtaccacct gntctggttc ctancccccac gacccttaca gtctaactgg 240
 gacacaaggg cttnaaatca aattgcctat cattaagata tacaanganc ntgagaaact 300
 gctncactta tntattaagg ngctctaaga cttagaaacn aaangcantg ctgagangat 360
 tcaaatatga ngggggnac tttnc 385

<210> 619
 <211> 869
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(869)
 <223> n = A,T,C or G

<400> 619
 gatatcccgg gaattcgcgg ccgcgtcgac ctctacttgt ttagacataa atgcagtcta 60
 gcattaaaga tcctttaaaa aaatgttttc ccaatgggta aaagacaagc tcaaataaat 120
 gaactctcat acatatgcca aaattgatga gtagataaat atttcagtag gtagttacta 180
 gctttctgtg tatgagtaaa catatgggag aaatttaaaa cactaaagta gactcaatga 240
 aagcatagta tcctatgtat tcgtttttca gaaatgtcta atgaaggaag gaaacaatga 300
 atgaatgcc ttattcctct tagagtgtcg ggacatgggt ttgcctgaaa acttcatgtg 360
 aattttatat tttgctacac attacacca tottagactt atacgtataa gacataaggc 420
 atatcttatg tcttacatgt ataataatct aagcagaaca aaaaataacg aaatattttc 480
 ttcccaaat ttttagaca gatggatttt ccggaagat gtgttttagct tttaatcctg 540
 tggttttgtg taccacctgg cacactagag tgttgctcta attcagtga ttgtaactct 600
 ggggtgaacag tggaaatact agggtagatt ttaaaaatgc taatgctcgg gcctcgctga 660
 agaccaaatt aattggaatc tctgngggng gnattgatct ttttataatc tttctanang 720
 attctaattg gcttccagg atgaaaacn ctgntggagc tnggaacctt ccttttagttt 780
 ggagaaaacc cgatgagggt ntnttaggen ccgcctnttt ttggcctggg ctccccccct 840
 tatntntttt tgggaangnc cnaattttt 869

<210> 620
 <211> 339
 <212> DNA

220

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(339)

<223> n = A,T,C or G

<400> 620

gngcgggct	cnccgtgctt	gctctcgctg	ccgacgtctt	ttttccacca	gctgtaggan	60
aagcccgaag	accactgggc	ccccgggtag	cccaggtacc	actggtcctc	ctggctcctg	120
acgctnoggg	tcttcctcgt	ggcgtagact	gccagcttgc	gagacccctc	agccctccc	180
cgcttttctc	caccccagga	ggccatcagt	agcgagctac	tgccctgggc	acaacctccc	240
agcangatat	cccgcgggtt	ccaatctgcg	aaaggaggac	cgccnagccc	gaaatgccna	300
gccagcnat	cactgccacg	ccgagccnag	cgctcgtgc			339

<210> 621

<211> 267

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(267)

<223> n = A,T,C or G

<400> 621

gggngcatg	gtccnngta	gccaagtaca	tggtcctcct	ggctcctgac	gctacgggtc	60
ttcctcgttg	cgtagactgc	cagcttcgga	gaccctcag	cccctcccgc	cttttctcca	120
ccccaggagg	ccatcagtag	cgagctactg	cctcgccac	aacctcccag	caggatngcc	180
cgcggtttcc	aatctgcgaa	aggaggaccg	ccnagccaga	aatgccnagc	cnagcgatca	240
ctgccacgcc	nagccnagcg	ctcgtgc				267

<210> 622

<211> 847

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(847)

<223> n = A,T,C or G

<400> 622

cttangntgt	cgactgacgt	catgcatgan	ttaaagcaga	ggtttggtga	aatttatgaa	60
aaatacaaaa	ttccggcttg	tcctgaggaa	gagccactac	ttgataactc	tacaagagga	120
acagatgtga	aggatattcc	ctttaatttg	acaaataaca	tacctggttg	tgaggaagaa	180
gatgcatctg	aaatatctgt	ctcagtggta	ttcgagacat	ttcctgaaca	aaaagaacct	240
agtcctcaaaa	atatcatcca	tccatactat	catccgtact	ctgggtccca	ggaacatgtt	300
tgccagtcac	cttctaagct	tcatttacat	gaaaataaat	tagactgcga	caatgataac	360
aaactaggca	ttggacatat	ttttagtaca	gataacaact	ttcataatga	tgcaagcact	420
aagaaagcaa	ggaaccacga	agtggttacg	gttgaaatga	aagaagacca	agagtttgat	480
ttgcaaatga	caaaaaatat	gaacaaaat	agtgcacgtg	gcagtacaaa	taactataaa	540
agcctgaaac	ctaaattaga	aaatctgagt	tctttaccac	cagattctga	cagaacatca	600
ggaagtatat	ctacatgaag	aattacagca	agacatgcc	aaagttaaag	aatgangtca	660
acacattaga	aanaagantt	ctgggctttg	aagaaagaaa	atgttccact	tcataaagaa	720
ggttgaaaaga	agaatgggag	agccngaana	ttttgccc	gaaattttcg	ggaaccctac	780
tggtatgggtc	nactgggttg	ccatgaatga	ataatggact	aatcnccaa	ttcctnggga	840
agggaat						847

221

<210> 623
 <211> 681
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(681)
 <223> n = A,T,C or G

<400> 623
 aaaactgtac tcgcgcgctg catgtcgaca ctagtggatc caaagaatcg gcacgagcga 60
 aaangctcan gcagcccggc tggccgccc cgctcctccc cccaggaaag ccaangtgga 120
 ngctgatgtg gctgcangag ctctgtttcac agccctcan gtgganctgg ttgggcccgcg 180
 gctgccangg gcggaagtgg gtgtccccc gtctcagccc caaggctgcc cctcaciaag 240
 cactggtggt ttgcctccac tgccaccttg ggctccgaac ccgctcccct gctgtggang 300
 cccaccgtgg gaatccagggt ccccagggtg actgcctgcc ttgccctcac tgcccactct 360
 gccacactt ccctgcctag anaccgggaa ggggctgtgt cgggtantgtt gccacactg 420
 atgtggcagc accgactgtg ggggtggacc tggccttgcc ggggtgcaaaa gtgggggccc 480
 ngggaaaagc acctgaagtg gccctgaaaa atccccctt aatttttccc caatttggg 540
 ctcaacaaa aggaatttgc tgaagccaan ggtaccaagg tcacccctaa ggccagggtg 600
 aaaaggtccc aaaattccaa tccccacct ttgggcttnc ctcttggaac cccggcccc 660
 tctcntgaan ttttaaaaaa n 681

<210> 624
 <211> 661
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(661)
 <223> n = A,T,C or G

<400> 624
 attggtctta ctgtaccacc ggggtggaat cgatggccgc ggcgtctaaa tatccgattt 60
 tttttttttt tctctttctg actgtccatg gacaaatgaa actaacttaa tctaactaaa 120
 aaacacaact atattttgaa gattttetat ctgcactcaa ggacactttc cacnccggtg 180
 ttgttacctt ttgggtctgt ctctgaacat gaaattnatc tcaagggatt ngatttctgg 240
 acctcctatt cctgctatgg gtttgatatt tcttgggctc cagggccact gttgcattgg 300
 gntgacagnt acctcctagc ccatancctc ctatcttggg aaacaaacct aacaactacg 360
 tgtaccttcc atagatctct gattgagttc cagtatnccg ttgctcatgg gcgattcact 420
 tgaatccgtn attggtgcca acaatcctga ctcatggggnn aatggatcct atcacgttcc 480
 cctgattngc aacccttgta tacatanatc taatcgcata gaatctagcn tnggntatgc 540
 gcggctacgc tatcagggtg tgntaactat ngcatggcta cgaancctga tcatgatcna 600
 gggctcatga ctcttatcag gggggttggg ccngcttct ttttcnnacc ttggtaaaaa 660
 c 661

<210> 625
 <211> 181
 <212> DNA
 <213> Homo sapien

<400> 625
 gcaacaatca gatcatgtta aagtaaatct ccattgccct ggatcacttc aggatttaat 60
 tgtccaagga gagcagggtt ctctgtgtaa aaaaagggtg ggaaatgttt gagagtaaaa 120
 aatacaaaat tcaaccggtc gaaaatacac cactccatto agtgccttac ccccataagc 180

222

c 181

<210> 626
 <211> 181
 <212> DNA
 <213> Homo sapien

<400> 626
 gcaacaatca gatcatgtta aagtaaactct ccattgccct ggatcacttc aggatttaaat 60
 tgtccaagga gagcaggggtt ctctgtgaa aaaaagggtgg ggaaatgttt gagagtaaaa 120
 aatacaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataagc 180
 c 181

<210> 627
 <211> 813
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(813)
 <223> n = A,T,C or G

<400> 627
 accaagctgg agctcgcgcg cctgcaggtc gacactagtg gatccaaagt gaacgtgaag 60
 gtgagcagag gagaacttgc gatggcaaag ttaaaaacaa gaggagatga tggctcttgg 120
 gtggcacagg atgttaaaaa aattctcctg tccttaagga gttactgcta tttgagtaat 180
 gtgccacttc cctacatagc cttctatgca gaaatgctat atttccactt cacaaccag 240
 aacgtgcatt ttattttaca tttagaggag gaacaaacaa ccagaaggca aaaactgggtg 300
 cattattttt tgcaattctc ttggaaagag ttcgttttta acttctgctc agacagcaca 360
 caactactgg gaatatatatt taatttcaaa tctgatgtgt gacatctggt aactcattta 420
 ttgctaataga agttttcaca ggaagcagca gtcaccagta gtcctatcta tttttcagtt 480
 ggcaaaagtgt tgtttacctt ttattggcct gcatcgggtg ctcttatcac aggatattta 540
 attagaaaac gcaagtagcc taacatagaa nagaaatgga gtggtagata atagtagata 600
 gaatggctaa atatttttat tacagtgtat taatatcact gnaatttatg gttaaaaatt 660
 atgtaatact caaaaggaat tctcagactg gcgaaacagc tggnaacag ctntcacagg 720
 gctttanact cctnttgagc tttcccctg ntggacttta gtcttccttt taencccgna 780
 gtnccattn nttaccaatt gtnccgggaa ana 813

<210> 628
 <211> 646
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(646)
 <223> n = A,T,C or G

<400> 628
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 atcccgtaat aacggaagac gaagaagagt cagaagagtg cttctataag gatcgggacg 120
 agactacctt agaggaataa aggaaaaaag cagaggagga agagtggtag aaggagtcag 180
 aagaaaccca cagtcggttc tgaacctgga gccttatcaa aaaggtctag ataaacgata 240
 gcgatctcga tatcgagctc aagaggtagg tttagagact tctcgtcctc gagagcgaaa 300
 ttgaagatct cgacgacgat aagaagttaa agtgtagagg gtgcttgagg agcgcggtga 360
 aggattctgc ggagggaccc atcgacgtag agacttgaag gcctactaag gtccacaaga 420
 agcccggctc tttctccgaa tggctcgagc gtacagtatg cgacgtcgat cggcagacaa 480

223

gctggcggtgta	gactcgaagt	gttcggggcga	atcgacttat	aatagtcgcg	cgctagtaac	540
gtaggaacac	gaagagtagt	cgaaagaaaa	cgtttagtga	gggaaaagat	tagggaaaaa	600
ggagaggctt	aataactaag	acacttggag	cctaggccaa	cgcgaa		646

<210> 629

<211> 617

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(617)

<223> n = A,T,C or G

<400> 629

gccccnccc	ccctcctnng	gcttatnngg	acagaccac	gtagtactct	aaatcttctc	60
ctacgccgga	caacggaccc	tataccaatt	cgaatcttgg	acactccgac	cgccggattc	120
tcttcccctt	tccgcttccc	ctttctgtcg	gtacccctcc	ctagtcgtct	cctacacctt	180
cgtaccgtcg	atatatagtc	gccgcggact	agcctattta	ggtgtcctag	actcgttatt	240
gatccactca	ttagtctagt	actatgcgtc	acgtatctta	gttgccctaag	agggagatta	300
aatcctccac	aagttccgac	gaattcctgg	actctcgtac	tagcaaaactt	tcttatgagg	360
cttccttgta	tatcttctgg	atgtttctcg	tgtcccggtc	ctccgctact	actagagctc	420
cttgccctat	ctctagaagt	agaggactct	cgggttcggt	ctccaaatct	agcgctagag	480
ctatcgctac	ccgctcgatt	ccccagcgg	aatcttgaaa	cctgaggtag	tacacaaacc	540
ctcncatct	tccctcgggt	gtccttctt	ctcatccccc	cttcccgcct	tctcgggaan	600
gaatctactt	tancttc					617

<210> 630

<211> 644

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(644)

<223> n = A,T,C or G

<400> 630

cnntcggcnt	gggttttntt	ctgagnnncc	ccccccccc	ccccccaaa	cttacacca	60
ccaaacactt	tccgccccct	acctaggaga	cattagaagg	gtttaggctt	cggcgtatag	120
taaagtccct	tacctcgga	gtagagaatt	cggtatttaa	attcagggtt	agaggctcgc	180
tcgttagatt	tatagttag	gtttagaatc	ggaaaccttc	gatcttcctt	agaagggtaa	240
taagtgaggc	cctaaatccg	tctaaccaag	gcgttaaggt	ccgtacctaa	acctagtctt	300
atcttctatc	aggcgcacca	atataggtag	gttctacttt	cgtataggcc	ttaaggaata	360
gttcggtagt	tatcgaaggc	actcctctct	aggctaggct	tttctcagtc	ttagtactcc	420
gggaccgtcg	tcgcanaaat	atcgatggac	ggtaggtatc	tccgcgttac	gcgtcgggct	480
agggatatag	agcgaattat	cggcgagagg	cggtcgctan	gaatcgggtat	caatatgntg	540
ttctttacc	tacggatatc	ggcagaaaac	ataaaacctt	ctnaccangg	ataagggtat	600
atcggacccc	taaaataaca	gtaacattta	gantactagt	accc		644

<210> 631

<211> 526

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(526)

224

<223> n = A,T,C or G

<400> 631

ccntcgggtt	gggttttttt	ctgagccccc	ccccccccc	ccccccccc	cccccccggc	60
cccatagccc	caccggnccc	acccaaattt	taacaaaata	aatntaccta	tcgntcacct	120
atcccnegta	tcgngtaggt	cggtagccgt	accgngatc	ncnacgattn	ttcgggtcgt	180
cncccttaan	acggncccg	agccnccgga	anaaatacta	cgagngactc	taatntagca	240
anaccgcg	tcnattanta	gcatccttag	tcttccaatg	ncgnggattn	ngaatccttn	300
naagttagcg	ggtagaacgg	gtcccgggtc	cccgccctct	tttcaattaa	cgccgggtac	360
aaantcgggt	tctaaattcc	ncacgaattt	ngncggcaac	attcncgggn	ccttattanc	420
cntttccaac	cccgatacnc	nagctcgatc	gggctttanc	gaatccgggg	tcnccccga	480
ngantccggg	tcctttgagt	ngctctagga	cggttacgac	ggagga		526

<210> 632

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(647)

<223> n = A,T,C or G

<400> 632

tttggngg	ggngctcat	ttgggtggac	tttttgggtc	gtaggaacct	ggtatgaggg	60
gtgttttgag	tttcttcttc	gtcgtctctg	ggaggttcgg	tttcgattga	gattcgggtt	120
cgtctttatc	ttacgaggca	ccctgatatt	gttgcgcttt	ggtttggttg	tggagagttt	180
tgtcctactc	tagcgggtca	tgccgatgat	atgtagcctg	cgtggcctga	tagtgatggt	240
gtgagcttga	gaggggagtt	gtgggtggtg	cgggcggagt	aggagggggt	ggagcaccgg	300
gattgggaga	tatagaatca	taagtgttag	gtataggctg	attgagcgag	ttcgtggaat	360
tcgtgtgggtc	atcataatta	gagtgaggat	gggctctata	tttcttagag	gacgcacggt	420
cgtgattcgg	ggtttgatgg	gtgttctctc	tgtgggcacg	attagcttgt	tcattgatgg	480
aaggaccata	ctgtttcgaa	tgaggattcg	tgtcttcgga	ttgttgtgga	tattgtggnc	540
tanactat	agtgtaaacc	ggaggtgggt	tgcctgtggt	gagtatccga	nnttcattcg	600
ganggtatgc	gtgcggagcg	gtcctttag	acattccgga	aaaatgg		647

<210> 633

<211> 630

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(630)

<223> n = A,T,C or G

<400> 633

tccttcgggt	tgggtttttt	tctgaccccc	ccccccccc	ccccctcgga	aggcctctag	60
gtccaccacc	gtctctctaa	tcctcaggaa	ccgatccacc	caaccaactt	actaatgtcc	120
tacagtaa	accogagaat	ataaaccac	acctaggcct	ccaatcctac	cagggaagca	180
agaagccgta	gtctagcgta	ttacgaaccc	gagatagaga	cggagatact	tagttttatt	240
ctctcggaat	aggaaagacg	actggggagg	gaatataggc	tagcgcgggg	ataggggcta	300
tggcggatat	gggggcgggt	cgtctcttta	ttcttctata	ccacgtcaat	aggaaatgtag	360
atatacctag	atgttcccg	agaaagagac	gttagaggtc	tccgaagcta	taaaggagag	420
gcgcgaagaa	acttcgtact	ctagctttat	ataggtagtc	gtctagtcc	cataagcgac	480
gagagatcta	ctagatttctg	gtatcgccgt	cgtatgtatt	cgaaatagtc	ttcttcccct	540
tttcgatctc	ctctctatac	tacatggnga	ttatagtcnt	aagatagtc	ggatattagg	600
atattagtta	tatgacgttc	gacgggacgg				630

225

<210> 634
 <211> 647
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(647)
 <223> n = A,T,C or G

<400> 634
 ccntcggctt ggggtttttt ctgaccccc ccccccccc cctccactaa gancttaacc 60
 caaccctata gtttactcgt ataggggaat cgaggagaaa taggaacgaa gagcgggtga 120
 taaagagaaa gtacttttct ttatatgtta agagcttagc gtaatgactt tcgttatatg 180
 gctagttagt tttatccggc gttatagggc ttagttctgg ttatctcggg tctaattccc 240
 ttagtatgct cgggagttta acgaggtcac gggatagcgc gtaccctttc taaggttctt 300
 ggaaagctat tcgttattta tcgcgattct cgaggtcgaa aggatcaagg atcttccctt 360
 ttactaccct agtcgggtta gcggtcggtc aaaactagt tagtacctt accctcctga 420
 aagttatagt cgaaacaacg tattagtcga aattatagcg gatagatcga gacggttctt 480
 tctcgggttc tcagccggta atccctctat ttgggggtct tctccctctt cccctttgtc 540
 ttccgcctta gcttccaagg ttccctcgaa gcgaggggtt ctacttaagt cgntagcgtt 600
 ccttataaac cncctacagg cagaccccct tgtaaacggc tcgggggt 647

<210> 635
 <211> 645
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(645)
 <223> n = A,T,C or G

<400> 635
 ccttcggctt ggggtttttt ctgagcccc ccccccccc ccgaaactc gccttaccct 60
 agatacccaa agaatagttc cactcaactt cgtctaagta aaactctaga acttccaaac 120
 ataaaagact tcgcgcggtt agctacacag cctacgggaa tctcacgaat ccgattcaa 180
 gtcccactct cgaccacacc ccggtatcgt cgttttccca taccaatgtc gaaaaataaa 240
 ataaaatcca gtcaagcccc acggtaagcg ggggtagggc taggcgaaga ggcaggaacc 300
 gttcgaggcc gggggctttc aaaatacaaa acaactactt aaagtttacc cttctaaag 360
 tcgggggcaa cgggttaaagc acgcctctaa agtactactc gtttcgagaa ggggtagtca 420
 tctcccgcat agagactctc gcgtatatca actcgcacgc cttctagcat tccgacggtc 480
 gccgcggct acatatcttg cggattagct ccgagggact ataggggtta ttagtctagt 540
 aaattctctt agaggatagt cggggtcgta gttaggcagt acgaggggac atggnctgcg 600
 tcgtgctcta ccttgacagc atactcttat aaacatcttt ttct 645

<210> 636
 <211> 643
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(643)
 <223> n = A,T,C or G

<400> 636

226

ccttcgggctt	gggttttttt	ctgaccccc	ccccccccc	cctagcggaa	aacaatcccc	60
accgagattt	tattaatcgt	aaaactcgcc	ttcggtacca	agtcttctc	cttcccgtaa	120
cctggctccc	tcctagnngc	tttacgaacg	tcctctctct	tcttacggct	cggagagtgt	180
tacggttaaa	tccggaggng	gggctaacga	atccaaggct	aactcctctt	anagtttgtt	240
gtccncncgt	ttagtaagga	tccgtggagg	gcgagtattt	gncccccggc	ctttattnta	300
tagttcccta	gtacgataaa	gntaccggct	atcctattac	agcggataaa	agttatttan	360
agggccgacg	tcnccgctag	acaggctaca	gctagnngag	gtaccgcctc	cgactantcc	420
gttgnntccg	acaaggngt	ttcggttaac	tccacaaact	cctccgcgca	ctctanggtg	480
gggacggcag	ttccncngtt	tagtgtgcgt	tatagagaag	ggcatttgag	ttggacgtta	540
cnttttaaca	taggttattc	cgtttaggtt	cttgccggcc	cgtgggggta	gtncnccggc	600
gcgttnntat	cggcgatttt	ccgcagtttc	cgtttccggn	tnt		643

<210> 637

<211> 631

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(631)

<223> n = A,T,C or G

<400> 637

gggttntctc	atttgggtgg	actttttggg	tcgtaggaac	cggtatgnag	gagtaggagt	60
cgctgggaag	actagaagtt	agctacggac	gattagtgtg	attccactct	taataacgag	120
taatcgttta	cgtcgggttg	gtgtttcggg	gttttgga	gtaagcgtag	ttgtggagtt	180
tcgcataatag	gtccccttac	ttcggcgatc	tcgtcttctg	tcggttagg	tattattggt	240
catccttcgc	attagtagta	gggttggtcg	gataaatcga	tagctattct	ttagaattcg	300
tagtcggaga	attcgtgtac	gaagtccttt	aagttcttta	agttcgcgag	taagacgtgt	360
acggttattt	tgctgcgcac	gtagggtgtc	tttacgggag	tttcgtttta	ggggtttacg	420
tagaacgtta	ttaagcacgg	taatacgata	gaggattacg	cgacgtattc	gtcttagaac	480
gtcgattttt	cgaaggcgca	tttgttatcg	aaggggagtc	cttgagagaat	cgagatatct	540
caagaatatt	acggagatta	cagatcggaa	ggctcccag	atcggacgta	ttaccggtct	600
cgcccgaaac	gagtaggtat	cntccggata	a			631

<210> 638

<211> 606

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(606)

<223> n = A,T,C or G

<400> 638

ccccccccc	ctcaaccatc	nattccccac	ctcaacgcga	attacggttt	cgaaagtcga	60
caataagtc	ggtcgagtag	agggaaatcag	gggctgggtan	aaaggaccac	gggcggaaaa	120
taccggtctc	cttccgggga	gcgacgtcgg	ggaaagggaa	gagagcggtc	tagttcgtag	180
gcaaacagg	cagaaaaagt	aagggttaaag	gtcggagggg	agaggatagc	tagtacgctt	240
agttcggggc	tcgggcgcag	ggccactttc	ctctttcgcg	ttcctttact	ctgcttacga	300
gttcaggctc	cggagttccg	cgccggagg	cgctgcgcac	ctaggaatgg	ggactcgctc	360
agtccecggt	tatccttcgg	gattctatgt	tttcgccgat	agacggagac	cgggtagtag	420
ggttccgctc	taccgccact	cgctgccttg	atccggcccc	ctccgcttaa	gggcgatgaa	480
agattaggt	ttagggctct	acgggacgag	gcatagggcg	ggagaagggg	ggaggggtcg	540
ggggtcgaag	ggantaagaa	atcgcantcg	cgcggggctc	gtagganccg	aaatttttct	600
cnncgt						606

227

<210> 639
 <211> 592
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(592)
 <223> n = A,T,C or G

<400> 639
 tccntcggct tgggtttttt tctgagcccc cccccccccc cccccgggaa cgagaaaaca 60
 atcccaccct accgcgggga gtgggttgna cgcttagttc tagaatcctc ggaatcgtcc 120
 tccggcgttg gtagttccgg cgattccgag tatgccgaag tgtatcgctc cgtctagagg 180
 ttggtatctg tttatcgcgga tgacgctatt gactcggatg ctttcgaagt agggggatag 240
 gcgcatagat acgcctccgc ggtgtcctct gaagtggccg catccgtgga cgcagcgtag 300
 acagctctgg tggacgataa cggcttctcg tactcctact cgggctatta tgtagagag 360
 gacttgtttc tgaacggata taccattagc gaaggggtac cctccgctaa cgcaggcgtt 420
 tctaacagtt cttccgggcy ctcgaattt agattgacgc ctccgcagca ttgtgggatac 480
 ctcttcggtt agccctcttt ataggatttc tcctccgcc cgaaganggg ctggtcgtcc 540
 ccggcangta tgtctagctc gaacgctttg ttactccttt gttttcgaaa na 592

<210> 640
 <211> 637
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(637)
 <223> n = A,T,C or G

<400> 640
 ctttgtggcg gtggntgtct catttggtg gactttttgg gtcgtaggct tatccgggtn 60
 gggctcccga agtagcttag gatcgccggc tagttccggt cccgcccgtc gaaagcgcgg 120
 ttccggcggc ggccccgcgt togttcgcgg gctttaccct catagagtgc caggtctcgg 180
 ttcttacggg ttcgtcggcg atagatttta cggcgagagg tccgtatctt cgcgcgttta 240
 cgttcgggtcg gcatctacgc ctagtccaca ggtagtttat ggcgccggagc gcgtgacgga 300
 gaggttatatc gggacgcgga agaaccgcct ccaaagtact agtacaggct cgttcgggcy 360
 tagatctcct cgctcggtcg gcggttctta cttctagggc cgctctacgg tttaaggcgg 420
 tcgttagatc tttagaaacta tactcaagtt tcagtcggaa gaaaggaaagt agagagaagg 480
 gtaaacgatt acctccggtt ctagcccttt ttactcgcat aacgggagaa cggggtccgg 540
 ctctcagata cgcctcgcga gacgtcgcga ttcaacttta acctccgcta gggcatccgt 600
 atacggttaa cgcggtaaaa gcgacctcgg aaacctc 637

<210> 641
 <211> 649
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(649)
 <223> n = A,T,C or G

<400> 641
 ctntgtggcg gtgggtgtct cagtttgggt ggatttttgg gtcgtaggna acctggtatg 60
 aggtctagtt tcttcaacga ttcttggttc agttacgcga ccctatcctt atcttacaat 120

228

```

gtcttctaca tcaggttcat caattaatat atcaattaca cattaacgac ggtgtgacgc      180
aatatgagaa agtatacatt aaggttatta tatattattc gcttaaaaag gttcctgaca      240
tgggacaact tcaccacca ttctagaagc cccccctcct gtaggacccc ctcgagttcc      300
ccattatctt agttcagttt tcatttttta accaggaggg tatcggtttt taataggtac      360
tattttgtca aacttttcag aagctttatc ttcaaatata cttgcaccat ctgtactagg      420
agcactaaact attcaggtct attacagctc aacagaaaat aattgaaatt aaacaacctc      480
agtatcgctc accataaacc catcgggctc tcacccatt tcttcataag ttctagagca      540
tcctgagctc tttcctatta cccttgatgg tactcatggg ctaatacccc ccgcagttat      600
aggtccttat ggatcctatg ctaccaccgg tctaaccctt tctatcacn      649

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<210> 642

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(645)

<223> n = A,T,C or G

<400> 642

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tccttcggct tgggtttttt ttctgcggcg gttactatta tcgattgtta cttgtaaagg      60
cgatactccc accgctcacg atattagacc tgctcctcta gaagcgaacg gcgataggtc      120
tactcggccg gcgaagacgg cgaacgggta ggaggagcca tatgcaacc taacggagat      180
tataagtact gggaaaaata ctagtattaa ggtagcgggt taagatagggt ggagagacac      240
tattcacgag cataagcact tagaagggtc tctcgaggag aggtaggcta cggactacgt      300
tccttcttcc tctagcctcg agaggagta tagatgatte gcaaaagaga atccctccta      360
tacgctggca taactagacg acgcgtcgtc gggaaatctc gccaaacctc ttgcgacctc      420
caaaaaggaag attgtcgttt catagaacgc taatactccg ggtcttcccg aatcatagcc      480
gcatatcggt aagaagacgg taaaatcgcg cgattctaac aagattctgt agacttaagg      540
ctaagcacta gaagcgatct cgattccgga tcttaagatc atactaatag ttcggtcaca      600
ccagacgacg attagccact agaagcccta ctccgtngaa accgg      645

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<210> 643

<211> 586

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(586)

<223> n = A,T,C or G

<400> 643

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ctttgtggcg gcggtgtctc atttgggtgg atttttgggt cgtaggaacc tggatgcag      60
ggtccgcccg gaattaaaag cgggatcccc aaaacgnngn ttcgcaagaa gagaagaatc      120
atagcगतag anctttcata gtacaaagggt aactaagagg aaaataatgc agattcagaa      180
ctagttgcca aattagaact cgattaggcc aaggatccga gcctggcgct atcacttcgg      240
gacttaagct acggtagagc agtcggtcct gaagcatagc tcccgtagga cgtaggaaac      300
tagtccggca cygaggacat actctcgagt ctcggaacgt ctatttagaa tataaacgca      360
ttaacctcag aaggcgccga cgcggttact ctctagggaa ctatttcatt ccttcggag      420
ctcccctatt tttccaacac atataccggc aaaggaaaat cttntgtcct cggctctaaag      480
agagggaaaa aaaacgatat ctaggttcgg gtttatocat ttaaaaanat ngacgcgact      540
actccctttc aaagggagtt tccccttagg nagagttcaa cngaag      586

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<210> 644

<211> 646

<212> DNA

229

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 644

ctttgtggcg	gtggttgtct	catttgggtg	gcatttttgg	gtcgtaggaa	cctgggtatng	60
agggctattt	gacttgtttc	tcaaatccca	tggtatggtg	ggtggcgtgc	ggggtggcgg	120
tcggttcggc	gggggtgggg	gtcgtcctcc	aaaggagttg	ctagagggct	tttagtggtt	180
ttagggcggg	aaggggttag	agcggagaga	cgtcgtcgtg	gaagcttctg	gcggagcgcg	240
agaaggtagt	tagcgccgg	tcggaagatt	ctcagaattc	gagaagaggt	agtggggcgc	300
ggagagagag	tttctaagtc	taaacgtaga	ggtcgtccta	gtcgggccgg	gagtagcttt	360
taagctagag	gtcggaggtc	tcgttttagc	tccgggctct	tcgggcagta	tcctctttct	420
cgaggaacgg	agcgaccgac	gtcgtagccg	gacccgtcta	tccttacgtt	tagagatacg	480
ctcacctcca	cgggcgtata	tgcccgtata	cgtataaacg	cgtaatatatac	tcgcgcgtaa	540
aacacgtata	cactatatac	acgcctcgta	cggaccgtat	agcgttatatac	gcgcgcgtat	600
attaatttac	acttatatac	gcgttaaacac	gatatatcac	acnccg		646

<210> 645

<211> 654

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(654)

<223> n = A,T,C or G

<400> 645

nccntcggct	tgggtttttt	tctgaccccc	cccccccccc	cccccggtcg	acaacgtgcc	60
caccgttgcc	atcccagcat	agctggttcg	ttctgtttta	ttcttagtag	tttagttcgc	120
ctatagtcct	tcgtctatcg	tctatcattt	aaggagcggg	ggctcgtctt	ttagggcggg	180
tatcttaggt	attcttctgg	tttcggctgc	cgtctcggag	tctggtcctt	ttgctttcct	240
ttcttggtcg	aacttcgtgt	ttgatcgcgt	tgtttctttg	gggtcgtcat	acctaaagggc	300
cacttcgcca	acaaacaagt	ttgtgtagtc	gtttctatta	gggttcgctg	gccggcgctc	360
ttactggttg	gcgattttta	acgcgtttgg	ttttaatttg	cttcctcccc	tagggctcgc	420
tcggtcttct	ctctgttcgc	tgtctctcgtc	cggcctttgg	tgcggggata	gctccggcta	480
ttancgtgcc	gtgtccgtgt	ggnttttgtc	caatgtgaag	gcctaggggt	gcgggcttct	540
ttggccatgg	nttccctctt	tgtgancctt	aggggtaacg	antcgttaatt	naaggtcggg	600
ggttggnata	cgttntangg	gangcctgng	tccgntattc	cttgttttgg	cctn	654

<210> 646

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(645)

<223> n = A,T,C or G

<400> 646

tccttcggct	tgggtttttt	tctgagcccc	cccccccccc	ccccacgcc	aagtacacag	60
accacacaaa	acaaacgtca	acacaacttc	gggtatacgg	accttaagag	agaccccgta	120
gtagacccta	ccacagccat	ccaatagtca	aacaacaagg	gcgcacccaa	tccatccata	180
gagctatcaa	acaacggagg	ggaaaggaaa	gagcagggtc	aacttagcag	agatcgaagt	240

230

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cggcactaat tcctttcaag tactcgctcg gctttagtgg cggggtaaag tccgctctca 300
aagggccaac gaggttttaa agcgaccccc gtatcgagtc ttcttctgtat tcattaaggc 360
gttaaaggta cgagacctag aagagagtag aattagccca ccaaatcgcc taaaccggca 420
aaaacgacca aaagtcaaag acccttacia atatacactt aaaacgcaa ccccaaaaac 480
gcgatcagta acgcaogtac ctttcccacg cttttctttc ttctactctc caaaacaaac 540
ccgaatattt agcgcaaaaa atatacggag gagaattaga agctattacc cgaaaaaaa 600
ncgganangg antaaatngt gggaatana cgtttggttt ttctg 645

```

<210> 647

<211> 753

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(753)

<223> n = A,T,C or G

<400> 647

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accttacctg gtacggggcc cccctcgag ttttttttt tccaaataca actcagattg 60
tatacgaaaa gctgataata cattgacttt tgctgtttta atcccttgag cctttgataa 120
tgattttttt tgtgttaaca attgtagtat ataaaatcgg attcaccatc cttctgatgc 180
catattgatt agtttgattt tatggtgatg ggatcattgt gtgttaactg tattaagaag 240
aaatggattt gattgacttt gcatccattt ttatctgtgt tactttcatg ttttatttaa 300
aagcatttct ggaccagaat aagttaagtg gtataatttg ctttttacac gtttatataa 360
ttgaagttag caatgtggca aaatctctaa tggaataaaa atgcttcaga atgatgacat 420
aaatctgagc tatttcttgc ctggagaaca agtggtattc ataataattt aatagcttct 480
gaggtgtttt gttcatgtga tgaaggctta tccacctgt atcaattcat gggctctgct 540
ttgtttaatg tagtcagggt gtttaatacna gacttaagag tcatctact gtgataagt 600
gtgagtgaag attacatgtc ttangaaaat tatactggga atatctctga cattaatggg 660
tttaaattgt ttaaggctag gggatgatgc aatgganaan atncttccaa angtttctg 720
ttgtttatat ttgnggaagn catnaagana ccg 753

```

<210> 648

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 648

```

gatatcccg ggaaatgcg aggcctttng gcttacgtgt ttaccgcgta gggcaaagcc 60
ttgncaaatt cccggccagc ggagcggcga ggtggtggac tcacgggaag ttaaacagcc 120
tcgtcggcgt cctcgaggct ccaaaaccag gctctaggcg gggacgactg cagccgttat 180
ggaggccacc gcggctacgg ccgcggctga ggcctcccca ggtggagcgg tggcctggag 240
gggaatcttg atcctgggcc agccacctgt caagaggagg cggagcgta tgcctctgga 300
agactggatg aatattctcc aggagcctga cgaaggcgaa gaagtctttg cagaggaaat 360
tgaatgctgt ctgatgctac aat 383

```

<210> 649

<211> 349

<212> DNA

<213> Homo sapien

<220>

231

<221> misc_feature
 <222> (1)...(349)
 <223> n = A,T,C or G

<400> 649
 cgattgtnta cnagtcttag agtaagctta agntcgntac cgagctcgga tccactagtc 60
 cagtgtgggt ggaattccat tgtgttgggt cactagtaaa tggatttagc tagacanagg 120
 anatttacc tttccattt agcacagtga gganaggcta nacagctagg atgcaataaa 180
 aaaaatttta atgagaaatg tgtgtggtag attaattcta ttaatctcaa gttatagatt 240
 aaaaaattta agtaccncat aaatgccatt tgcctttgct aangntacat ttttatgaan 300
 aangacntg catacnaat ganatactgg actttnggna cttgangga 349

<210> 650
 <211> 306
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(306)
 <223> n = A,T,C or G

<400> 650
 catttgtttg ggagcatcct tccatcagct cccatgagaa attctctgtt gggtttaagc 60
 aatccccaaa tatatcata tgcacatgaat atatcatctc ctcaatgtcc agcattagca 120
 gacaagatga gtgctgaaga tgatataact cctacctctt atgtaggcta gaggtaaagt 180
 ctggctctgc tgactgtggg gacataccga aaaggaatgt gggttaatat cagangacct 240
 cctgcagat ccganantca gggncctggac tttctgggan aggaagcnaa aagttatntc 300
 tgaacc 306

<210> 651
 <211> 769
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(769)
 <223> n = A,T,C or G

<400> 651
 catttgtttg ggcagggtca tttctaaggc atgggctgga agcttttatt taaaacttta 60
 catgtcttag aagcactctg gttgttgcta ggcagacaat tttacatctc ttgctataacc 120
 agttgcatga agttcatcat gcatattggc tgtggaaaac cttaacagca tcatgtcata 180
 aggtttcagt aaggttttaa tgaaatcatg tattaagcac ttagtatagt gcaccttaaa 240
 tgttagcttc aaaacaatga caacctaaact aatgttgaaa gaagcttggtg tttgtaaatt 300
 atgtcttatt gaaagatgtc atcaaactct gttatttcta atcccttaaa gtctctcaat 360
 gtatttcttt ttgccatatc caatgacagg accttagttt aagccagtgg ttctctcaac 420
 ttctaattcca gagatacctg ggtgtcccca agaccttttc agagcatcct tgatgtcaaa 480
 accattttca taataatatt aaaatattat ttgctcattg tactcttatt ctctcccaaa 540
 tattcagcga gttttccaga agctatataa catgtggtaa catcttatca ctctgacgat 600
 taatagaata tngnttttg gattcttgng tttaaaattt tctcactttg gggttctaatt 660
 atggnnacga ttaatagata tggncctccat gaccagangg ctttaaagca ntcaataatt 720
 ttttaagagac taagnactat ccttttaaaga tngngaactc catcttaatt 769

<210> 652
 <211> 267
 <212> DNA

232

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(267)

<223> n = A,T,C or G

<400> 652

nnangccctt	taaccattgn	ggcctccacg	cnntggcggc	cgctctacaa	ctagnnggatc	60
cgcnaactcta	gnanaangat	tggctcttnt	ggngtggggc	ggncggggctg	gggcgttaag	120
cggggctggg	cgcgcgccgn	ggttgnacna	ggcgccgccc	ccncacacn	cccggagcac	180
cctcnttgc	gcctntcccc	gctcaccccc	cgcgcgccgn	tccgcttttt	ccncacccan	240
agcnctnttt	atctntgtct	cctccgg				267

<210> 653

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 653

cccnttnacc	cattgctgga	ctccacccgc	gtggcgccgc	ctctanaact	agtgggatcc	60
ttncnatgag	atgngcgang	gaggacnnat	ttgctatnct	ggatggggct	gantcntnta	120
gctnctctag	cancagatgg	gttatcgagg	aagatgactc	caangggcta	nantcctatg	180
cncatcctaa	aanncanctg	ctgtnttcag	agtacgcgac	acatcatcnc	tnatgcattg	240
ntgancaaga	cgggcangtg	cttatccctca	gcgangatgc	ccttaaccan	gagctcgaat	300
ggacntatca	ccttanaggt	acanntnccg	caccacacac	cngcttgenn	cctgacgctg	360
gactggatcn	cttaggccac	caatnccccg	tttnccacat	ncctgggacn	ctananatac	420
tcganggggg	gcccgggtanc	caattcgccc	taatactgag	ccttgntacg	nacgctnact	480
ngngtccta	ttanaacggt	g				501

<210> 654

<211> 710

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(710)

<223> n = A,T,C or G

<400> 654

gcgnctttan	cncatgctgg	gctccacgcg	gtggcgccgc	ctctacacta	gtggatccca	60
acactgagtc	caccacagna	aaactcanca	ccaggcagac	cccacaactg	cagaatccag	120
gctgcaattc	acagactaat	cntctagacc	cacctcagta	ccagatggta	ccacacagct	180
caaggnttta	ggtttgcgtg	gtanactcaa	tctctatctt	tcaccactgc	cagcctgact	240
tcagagatcc	tgngctctgg	acagtccctca	gtggcaggca	actctcagga	gcctcaggnt	300
tttggcacat	cccagnacca	gccagctgcc	acaggccctg	accttntanc	aacactgccc	360
atgtattcca	gacttctanc	ataccacagt	gccatgctga	ttgcatctat	agangctcag	420
gtgencctca	aanctgtgcc	tgtctcgagna	ngccccacgt	ctctggcatg	ccccaatgcc	480
atgngtggn	acanttgact	tctgggcatg	ntgggaattcc	ctaccactga	ncctgaccat	540
aggnggganc	ccattttttt	cgaggggggg	gcccggcccc	caattccncc	ntatagnag	600
ncgtanttac	gcgcnctta	ctnggccngt	ngtttaacaa	cgctcnntgan	ctgggggaaa	660
cccctggng	cnacccaaat	taaacngcnt	tgcannacat	ccccctttcg		710

233

<210> 655
 <211> 202
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(202)
 <223> n = A,T,C or G

<400> 655							
cccccttttccc	ctttcanccc	ccccgttttg	gngccgccc	acacctactn	catccacca		60
cantcgacca	cccgagcttt	tttccgatcc	cancatcnat	gngattttn	tctntgcntg		120
ctgngcctgc	acctttgnta	ggtcaagcct	ggcccatctt	cgacaacttc	ctcatcacca		180
acgatgaggc	atactctgac	ga					202

<210> 656
 <211> 308
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(308)
 <223> n = A,T,C or G

<400> 656							
gctgntgaaa	gaccacaccg	aaaaactctn	ctttccgact	tccacatgat	gatcngcatg		60
tggtggtgag	agacttatca	tgacgacatc	gcttccnacc	atcgcanccn	ctgcccgaagc		120
ccattcatgg	aggcctgggn	antttctgtga	ntgacntnga	cnctanacnc	tnccactgtn		180
tgctatccag	acttgnttng	aatatnttat	tggcnaaana	canttnccga	atgctgtgnt		240
tgnnccattga	angatctgat	cactatgaga	gggtgaggac	nncctgctng	ctggcantnt		300
ntaaccn							308

<210> 657
 <211> 696
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(696)
 <223> n = A,T,C or G

<400> 657							
accntttcca	caatnctggn	ctccccggcg	tggcgccgc	gtcgaccagc	aacctcagct		60
gtgggtcttg	ttacagtaat	gagttactgt	aaggaaagtg	tgacatttcg	agcaatttga		120
tttgtttaaa	aactagagca	gtttcagggt	tttcttgta	aatctgtctt	atgtgtcttc		180
aatgttcttt	cttgaggagt	agagaaagga	attgttagga	atgatgcata	aacctatggct		240
tattttatct	cgctgccacc	cataatcaga	gcagattctt	gggactatga	ccctcatgga		300
gacatgacaa	ttgtgtgtgt	ggtgggtggg	agaaaagagc	tgggaatttt	taggggtctag		360
agggtccaat	caggactatt	ttatggagct	ctgctcacca	actttaagtg	agcaccaggg		420
gtngaaagc	gaatcttggg	ntcaaaanaa	caatggnaag	gggtaagttg	gtatnctgaa		480
ctggccactt	cggactctta	tttaactggg	tattctcant	taaggaggcn	ngggtggtct		540
tggtctgtna	aggaagcct	gtgcaatgga	atgactttaa	aaccccccat	taaaaaaaaa		600
angntataaa	tcttgggtct	taanaangaa	gcctgggttc	tnntanccca	ttttncctcc		660
gggaaggnaa	atnttcttag	gnaanggaag	ggaagg				696

234

<210> 658
 <211> 698
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(698)
 <223> n = A,T,C or G

<400> 658
 ctggactccc cgcggtggcg gccgctctag aactagtgga tccgtgttgg ctcaattctc 60
 aaggctgttg ctgtgcggcc tgttccccac acgtgctgct cagctcaggc aagcacccag 120
 cttgtgttgt ttcatgtcta gcgtggaggc ccctcctcca ggtcgtgct ctgtgggggtt 180
 cccatacact caggctccta ggaggagtcc atttagaaag ccagggtttt tctcagagtc 240
 ttagttcctt gtgctgtcat ccatttcaca cgacttgggc cctgctcggg gcaacacagc 300
 aagagaaaag acagggaaaa taagagaggg accttgcaca cacacgctct ggaccacaga 360
 gccctgtgcc cagctcctct gtcaatacag gtggaatctc gtgcaggatc gcagggggtct 420
 gtgatgccac caaagagcag gccgggacag ggtaggaga gaaaggagag ggaagtgggg 480
 gtttctccta cgcactctta ttgcagagg gaaaggcggg ttgtattgg ggttgcgggt 540
 ctttgacccc acngcacagt tgtgagacac ccccatcctn agatcaaagc cccacataca 600
 gcttggggaa aaacaaaacn aaacaaaaca aaaacagtaa acctccatgc canttgttgg 660
 gnaagttttn aatttncttc ccnaccan cttgcttc 698

<210> 659
 <211> 750
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(750)
 <223> n = A,T,C or G

<400> 659
 ncaantggn ctccaccgcg gtggcgcccg ctctagacta gtggatcctc ctcatgggcc 60
 tggatatctc tgaacatatg atgaacattg cttatgaaaa attatttgta ngaaaattgt 120
 gaggcctaag aatgntatth tcttttagtg atggctcttg ttgtctctg taaggnaactt 180
 gtgggcactc gtaagcttgg atctctttta tctaatacca gntttgagat tttcttggcc 240
 ccatagatga attaaaaactg gcgtacttct tgtttacaag anggataagt ctccataggt 300
 aagtcttttg gggtcccaag tcaaaaagat gagggattta ccagttctct aaccttggt 360
 gcccagact ccaaaactttg ccttctagtc ccaagaggct atcaaaaagc aaaggccatc 420
 ttccaccttc ttttccanaa cagcacacat tccagacagt acttgaaagc aggaacctcc 480
 ttatccctta aaaacctctt ggaancatct tccctctctt gcttctacta tgcttggccc 540
 acctancatt cncntttttc tggaaaccgg aaaaancttn tgacttnngt tggctacatt 600
 cagcttggcc ccctacaatn tgggtttccat ctgccctaan gaaattttta agggcacttt 660
 tttnttggcc cctgacttct nnttttttagg gctttccccc angctttgcc ccttttggtta 720
 aaggggttat tttccttccc cttttggaag 750

<210> 660
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)

235

<223> n = A,T,C or G

<400> 660

tcggatccac	tagtccagtg	tggtggaatt	cgcggccgcg	gtcgacgggc	agtagtggtg	60
tgcntntcta	aatgttataa	ttatttcaga	attactctgc	cagaaaagtt	tgatcataca	120
tagaagagtt	tgtagctaac	tttgaaagta	gtggaaagtg	gttttcacgt	attgtttggg	180
ttaatttaat	tttgattata	tttggttttt	agttcaggta	atTTTTTgt	tgaaaacttc	240
aaatgacaat	ttcttcatgg	ttactaaaga	tcactcatgt	ggagtagttt	cagatttttt	300
tctgaataca	tgtattactt	ttagagatgt	aaagatgtga	aattactaag	agagaaaccc	360
atgtgatattg	tttagtggt	caaaagtcgg	tagctccttt	gacctaagt	gccactgata	420
gttaaataga	tactgaagct	atgggcaggc	tggattgata	agaaaaaagg	agacagagaa	480
atgggaaatt	ggcgaagac	tgtgcaaata	ggaaaaggag	agagcaacag	aacagaatta	540
gtaccacagt	ggcgaagtc	cacctcagg	acttccatct	cccatctcct	gaagaattca	600
gtaacagttt	gcaaatggtc	aacacaatca	tttagtgatc	ctgggttgata	ttttcaatac	660
tttctgggga	tttcttggt	ggnttcaaaa	gatgatgctg	atagttttat	tgcccctgaa	720
ggtattctga	agnttancat	aatttattgg	tcagtaaaat	atTTGaataa	aagngganga	780
aggaaaatct	ggcntcttat	tttgggatnt	cngcnggggg	aangaggata	taattnaccc	840
cggccttgg						849

<210> 661

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 661

aacttaagct	tggtaccgag	ctcggatccc	tagtccagtg	tggtggaatt	cgcggccgcg	60
tcgacctcca	ttcgtttctt	gtcctttttt	ttcatttttt	ctcatgttct	attcacttta	120
ggtttctaag	ataaatatta	taaaataatt	tttacttata	aattattcac	tgataccctg	180
tctttaacat	gtgaaatgaa	ttcaaaaagga	atcttaatga	gaaataatat	actcatgatg	240
tttaatatag	ttgatttcga	aataataagc	cctctgaagt	cctaagttaa	aaataaagca	300
acttggttga	taatttttca	tcaagaatgt	atctgagtct	ctgagtaatt	attagtagga	360
atattccatt	atcacaatta	cacagtataa	gctatttagt	ctaactttac	caaaaaaggg	420
agctacttca	acactgtgtg	agacttttaa	tgggtttgca	ttgggtatgc	actattagca	480
agataaccta	ttttacagca	gtgtttntta	acctttccca	tttatttgaa	aggcagctaa	540
gatatagtag	ttaatntaan	gggctgatgc	atttatatta	catgtagana	atgggagata	600
cnaaaggagg	nggggggana	tnntttgnat	tcnnaagctt	cnttgncaat	taa	653

<210> 662

<211> 646

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 662

aaacttaagc	ttggtacccg	agctcggatc	cctagtccag	tgtggtggaa	ttcgcggccg	60
cgctgaccca	gggacaggca	gccagnctg	gggtcaccag	ggccccctct	tgggccctcc	120
aanagcaaca	gtactggcaa	cagctgggat	ttgctgagca	cagactctgc	agcaggctcg	180
gttagctctt	ctgtgcctgt	tccttcatac	catctcaccg	cccatccatg	agatgggtcc	240
agctgttttc	agatgagaaa	atggcacagg	aagctggtaa	gtgacagtca	gaaatgaatg	300

236

```

ctggcagctt antccttgga cccaccgcag tgcaggacct tgctcaacag ggatcaccct 360
tgtccgccac ctgttcacga ggccaccacg ggtttgtgtg gtcatttgtc tcctttcatc 420
tgcttgccct caaccagctg ggtcattagg gctggggaac ccagacccca cacagtcctt 480
ctcccagang ccagacacan nctncgccac agnaaggact tcagtccccg aancaaatgt 540
ncctgggcgt anaaactgna gggnccccaa tccctgggtg ggtactgctt tgcactggng 600
gaattcaccc ctcattgnna acctttccct nttnncccc ctaaac 646

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<210> 663
 <211> 650
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(650)
 <223> n = A,T,C or G

```

<400> 663
aacttaagct tggtagccga gctcggatcc ctagtccagt gtggtggaat tcgcggccgc 60
gtcgacgtcg acgcggcgng ccgtttcgac gcagttgata catattatta tatactacat 120
nggttttcta gaattaaaaa attaatgtgt agtgccagcc ctatagtgtaa gttacatata 180
tcaactctat ccaattttgt cagccataaa acttaccttt ttacataact tctaactcta 240
acaatgtgag aaatgtagat cattgcaatt ataccacaa ggcagatggc tacatgcaga 300
atggatagca gaattctagct acttacgcta gccacatggg agacgttttt tcctttgttt 360
ttgcaaaatt gcaatataag ttgcatatcg ttagagttaa aagatgtaa gaaccatag 420
aagccagtga tgaaggacat ttatatatttc acctttacaa angaccttaa aattgcctat 480
gtggagcaga aactggagga gggcnaanc atcngtaaaa aaaattttgn tncattttgg 540
atttgggcac cattattacc tccccaggtn cctttttgnt ttaacctttc ttttaaaaaa 600
aataattcnt aatttttggg caaaaaaaaa caaggttttt attTaaattt 650

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<210> 664
 <211> 678
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(678)
 <223> n = A,T,C or G

```

<400> 664
taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttta aaatgttagt ttgtcttccg ccattttctac 120
agaaagctgc aatttcaggt tttcaacctt ataggtgata ttttaagaaa aaaaaaagca 180
atcgcaaata gccccactgc ttttacaat cattttttct cttctaggta tagcctgtca 240
ggtggccata tgtaattttt gacatctcta ggaattttaa tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa 360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt 420
anaattattt taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagt ggaacacaga taaagaancc caaaataaat 660
cctatatatta cngccccc 678

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<210> 665
 <211> 694
 <212> DNA
 <213> Homo sapien

237

<220>
 <221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 665
 cttttcaaatt cttttttnct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60
 gacatctcta ngaattttta tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120
 cttaagtggg gatttatgta tttctcaagc aagtgattaa agcaaaacta ggcacgattg 180
 aaatcaagat cttttaggca anaaagtcac gatgagtttt agaattattt taggactctg 240
 tggctttctc ttcatagaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat 300
 agccaaagca aactganca aaaagaacan agcagggaag caacacacta ccngaattca 360
 aattatacta ccagggtgta gtaacccaaa cagcattcta ttggcataaa atagacacca 420
 agaccaatgg ancagaataa agaaccacac aaataaatcc atatatntac cgccanctga 480
 ttatcaataa cnaacaccaa gaacatatnt taagggaent nctattcaat aantagtgct 540
 ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agaccctat ccctcaccat 600
 acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660
 atnaaancta ctattaagaa aacagatcnc nccc 694

<210> 666
 <211> 705
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(705)
 <223> n = A,T,C or G

<400> 666
 tttaaaaatt tagatacact angaaaatta ttttagtata agaagaatat caggggggtgt 60
 agtactcatc agagctaaat gagagcgctt taaaaatgtt agtttgtctt ccgccatttc 120
 tacagaaagc tgcaatttca ggttttcaac ctaatagggtg atattttaaga aaaaaaaaaa 180
 gcaatcgcaa atagcccccac tgcttttaca aatcattttt tctcttctag gtatagcctg 240
 tcagggtggc taatgtaatt tttgacatct ctaggaattt taatagaacc agaaatgggt 300
 gccagagata tgcctgcaat aatcttaagt ggggatttat gtatttctca agcaagtgat 360
 taaagcaaaa ctaggcacga ttgaaatcaa gatcttttag gcaagaaagt catgatgat 420
 tttanaatta ttttaggact ctgtggcttt ctcttcatag aaatagaaaa aaaaattgta 480
 taaaaccaca aaaggtcctg aatagcccaa gcaacactga acaaaaagaa caaagcagga 540
 agcaacacac taccagaatt caaattatc taccaggtg tagtaaccac aacagcattc 600
 tattgggcnt aaaatagacc naagaccaat ggaacagaat aaagaaccca aaataaatcc 660
 atatttttac agccagctna ttatcaataa aaacnccaag aacnt 705

<210> 667
 <211> 817
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(817)
 <223> n = A,T,C or G

<400> 667
 nnangacttt tgtggtntta tacaattntt ttttctattt ctatgaagag aaagccacag 60
 agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120
 tcgtgcctag ttttgcttta atcacttgcg tgagaaatac ataaatcccc acttaagatt 180

238

agtgcaggca	tatctctggc	acccatttct	ggttctatta	aaattcctag	agatgtcaaa	240
aattacatta	ggccacctga	caggctatac	ctagaagaga	aaaaatgatt	tgtaaaagca	300
gtggggctat	ttgcgattgc	tttttttttt	tcttaaatat	cacctattag	gttgaaaacc	360
tgaaattgca	gctttctgta	gaaatggcgg	aagacaaact	aacattttta	aagcgcctctc	420
atttagctct	gatgagtact	acacccctga	tattcttctg	atactaaaat	aattttccta	480
gtgtagtcta	aactttttta	aaaagacatg	taatccgcgg	agtttgtaac	tcaaaacgag	540
tgcatctagg	aggtatcgca	agccgtttct	ggattaaatt	cccagctagc	ttgcttgctt	600
agcaggggcg	ggnaaanaag	acatctgcag	cctaggggaag	aaaacctttc	gcattgttct	660
tacgtgttta	cgttattttta	tttcctanaa	caaggcngaa	ttgggactcg	aatgggttcag	720
ttgggggtggg	ggatccccctg	gtncataaaa	ngtcanaaag	anggtacagg	cggaacncca	780
agggtcgtcc	tgcatttana	ctcgaatttt	tggtgcc			817

<210> 668

<211> 826

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(826)

<223> n = A,T,C or G

<400> 668

cgggggggnnt	tacgtctctc	tggacgcttt	tattgtacca	gggcgatccc	agcccaactg	60
taccattcga	gtccctactc	ctgccttgct	ctagggaaat	aaaataacgt	aaacacgtaa	120
gaacaatgcg	aaagcgtttt	cttccctagg	ctgcagattg	tcttcttcac	cgccccctgct	180
tagctagcta	gctagctggg	aatttaatcc	agaaacggct	tgcgatacct	cctagatgca	240
ctcgttttga	gttacaaact	ccgcggatta	catgtctttt	taaaaaagtt	tagactacac	300
tagggaaaat	tatttttagta	tcagaagaat	atcagggggt	gtagtactca	tcagagctna	360
atgagagcgc	tttaaaaaatg	ttagtttgct	ttccgccatt	tctacagaaa	gctgcaattt	420
cagggttttca	noctaatagg	tgatatntaa	gaaaaaaaaa	acaatcgcan	atagcccact	480
gctttttacaa	atcattttttc	tcttctaggt	atagcctgtc	aggtggccta	atgtattttt	540
gacactctcta	ggaatttttaa	tagaccagaa	atgggtgcc	gagatatgcc	tgactaatc	600
ttaagtgggg	atztatgtat	ttctcaanca	agtgatttaa	gcaaaactag	gcacgaatga	660
aatcaagatc	tttaggccag	aaatcatgaa	nanttttana	attattttan	gaatctgtgg	720
cttctcttct	taaaatngaa	aaaaaaattg	tttaaacc	naaggtctga	atacccaagc	780
noctgaacn	anagaacaan	gccggagcac	cccctccaa	atcccc		826

<210> 669

<211> 547

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(547)

<223> n = A,T,C or G

<400> 669

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tcagactttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatttag	ctctgatgag	tactacaccc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagtttag	taactcaaaa	cgagtgcac	tnggaagtat	cgcagccgtt	300
nctggatnaa	attcccagct	tgctngcttg	ctnagccggg	gggcggtnaa	aaaaacatct	360
gcgcccngg	ggnaaaaacc	ttgcattgt	tttacgtgt	ttacgttatt	ttatttcct	420
nnagcaaggc	nggganttgg	ggactcgaaa	tggtacagtt	gggctgggga	tcgcccttgt	480
tacataaaag	ncgtccagaa	gagggacggt	tacaggcngg	ganctccaaa	ggtcagtccc	540

tgccatt 547

<210> 670
 <211> 232
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(232)
 <223> n = A,T,C or G

<400> 670
 cgaactatatt agactaccta ggaaaattat tttagtatca gaagaatata aggggtgtag 60
 tactcatcag agctaaatga gagcgcttta aaaatgtag tttgtttcc gccatttcta 120
 cagaaagctg caatttcagg ttttcaacct aataggtgat atttaanaaa aaaaaaagc 180
 aatcgcaaat agccccactg cttttacaaa tcattttttc cccaacacaa tg 232

<210> 671
 <211> 214
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(214)
 <223> n = A,T,C or G

<400> 671
 ctccccctcc ntccttcgct actnncatt ttcnnaaatt tntttcgcnt atgnnggaaaa 60
 acaccacat tnttcanctc gcacagaaca ngnnnggggtg tgtaaaatga agggcttccn 120
 cncctttctct tattnaanaa cactnaaana ggganggggt aaaacccgcg ngatntctac 180
 nctatcgcg gcgcttttgg ngttggctag aaga 214

<210> 672
 <211> 328
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(328)
 <223> n = A,T,C or G

<400> 672
 ngancagcgg ngtttaaacg ggccctctaga ctcgaggaga cncctgttgg atggtggatc 60
 acanntcgnt actactatac aggacagagt atcggganct cttggntgtt ggngcctgcc 120
 aaccactgct nctgttaact gcgtatctga agggactcgg actggcttca gaagaactac 180
 cggtcgaaat gnaccatgga tgattcncnc tagttgaaaa aaaactcagg cacatgtatt 240
 gccactgatg actagcgcca gactnctctc ggctctntaa cgagcccaca tgnrngtgtg 300
 ncncctgtgc tgnctccaga agaggttc 328

<210> 673
 <211> 223
 <212> DNA
 <213> Homo sapien

<220>

240

<221> misc_feature
 <222> (1)...(223)
 <223> n = A,T,C or G

<400> 673
 gggggc aaag ctggctagcg tttaaactta agcttggtac cgagctcgga tcccnagac 60
 attgtgcatg aaaatgcaaa ttgagtgtgg tctatantgc catcntcacc tntgncngc 120
 tcaaaacaac ngctttctgc tgcaatgggt agggctcctn acncacggtc gcnnacggag 180
 gccncttat cctcntcggg nnggatccct ngaagcatnt tct 223

<210> 674
 <211> 256
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(256)
 <223> n = A,T,C or G

<400> 674
 gnggggtcnt ngatgagcgc gcgtaatacn atcactntcn ggcgngntgg gtaccgggcc 60
 cccctcnaa gcggcgccc ttttttntt tttttcatn acatgataa ntcttnttc 120
 taaacagacc acaccactan agttcctttn ctttngtacg gaattgagtt aaagtagagn 180
 atacaatgca gggcttcnnc tctatttcac attccaggnt ggttcngnat ggatcggccc 240
 tgcctctcgc atgggt 256

<210> 675
 <211> 439
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(439)
 <223> n = A,T,C or G

<400> 675
 nnactagtcc agtgtggtgg aattccattg tgttgggctt gtatggggtt tttgtctag 60
 ttntttggga aatgttngtg ttactatntt ttggatatna tatatgatat gtatggccct 120
 tctatgggct cctcanacng aactcaacca ttttccaaa aaccnattcc tcctttccct 180
 tcatgactga gtgggtgttg tactatccng gaaactggga cattgtcctt cacatctntc 240
 ccttanctgc ctngtccnat tgatgtcttt gagctntgan atgtctttgt taactntctc 300
 ctncntctgt actgccggca naattaagca ccatntgtca caaaaagtat tgcgttacct 360
 tcacgnatct gttngttnc atncttgctg cttctccngn ggaaaatagg ctnttctggc 420
 aaccgaacng aanaaatac 439

<210> 676
 <211> 587
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(587)
 <223> n = A,T,C or G

<400> 676

241

```

ngngggcctn  attaagcgcg  cgtaatacna  ctcactntgg  ggcggaattgg  gtaccgggnc      60
cccctcaagt  tnatntgccn  aacctctctt  ttggaataac  aaaagggttta  acacatatgt     120
cctcataggg  acgcgccttc  acacnttcct  gacngcttca  tanacntcat  tncatatttct    180
cctcagnaca  agttnaggcn  gaaggtgagg  canacnttat  aatttccatt  tcacaaatnc     240
ggaagtgag  gctcaaagg  nttaaaaaat  aacctgatac  aantcataga  gccggtntct     300
ggaanaagca  ggagcaaagt  ccaggcatcc  tgatccaagc  tnggtccact  gccttccact     360
ctggagaggc  ttcatctccg  acaaaggaag  ggacntgagt  ggctgganaa  totcatggga     420
taaagacctc  agnatattcat  gctcctggaa  atcccatggg  ttgaacaaca  ggtntttggc     480
ccgtggttct  ntccctttgn  ccattcttta  accttggggg  aaatgatggc  ntctntnagc     540
nttttttttn  aaagagatng  aaattgaatg  attatngct  cattggg      587

```

<210> 677

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(444)

<223> n = A,T,C or G

<400> 677

```

gtggggcatn  attaagcgcg  cgtaatacga  ctcactatag  gggcggaantg  ggtaccgggc      60
ccccctcgaa  ggggcccggc  tttttttttt  tttttactgt  ccaaactntc  tatngatnta     120
gttgaactgt  ncaacgattt  catgaaattc  tatacacana  gccttcaggt  ccagagagta     180
aaacaaattt  aaatttnttc  accanattgn  agcagncana  agcatccnat  natatccgac     240
tacaatgaat  natatgctna  nggtanctna  tttaccact  ntggggtctt  tanggtctgt     300
cacaaactat  tttcgtaaac  atcnntttaa  antnggtga  atggacctaa  tnccagataa     360
ntctatttna  tntacccatg  catnccgtgt  gctnactttt  cgggctgtgt  tggcntactt     420
ttaggagaaa  attggtataa  atnn      444

```

<210> 678

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 678

```

actagtccag  tgtggtggaa  ttccattgtg  ttgggagcag  tttaaaaaaa  aaaaagacna      60
aatatacnac  tcttgatnaa  acataaagg  acagtggctt  atgaggaana  gaaaagggtac     120
ctnaggatgc  aaaantacct  accacatggg  aaccgttngt  ccacactcat  tccnnanaaa     180
accgagtcct  ctcanttnca  cacgtgtacg  tttcagttgg  gaagtgcttg  ccattactcc     240
naagcctaga  acottcacgt  cctgaagggt  ctggaagggt  tttcagattg  cttaaganac     300
gcngcccttc  catattntc  tccactacce  nggggaacgg  aacaaatgga  gctgcgacng     360
ggaagcgctc  cttccntcc  gaaogcttcc  tttcaaacct  gctgccttc  cnggcgaatg     420
gaccggaagg  tttntctngt  tcccttcanc  ccnaattact  tccctgngttg  aaaattggcc     480
tgttggtttg  caaatgcngg  aatttgttta  ctttctntcat  gtccgtgtgt  gnnncnaaccg     540
gctcncctgt  tgccctccct  tngaaagggt  ttcattcaggc  cccgcccttt  ctcttntaan     600
ngtcctaata  cggncnggac  cactcgggga  aaattttttt  ttttcgaaaa  gccgccccnt     660
ccgtccggct      670

```

<210> 679

<211> 449

<212> DNA

242

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(449)

<223> n = A,T,C or G

<400> 679

actagtccag	tgtgggtggaa	ttccattgtg	ttgggagtag	gtctactaca	ncctacttcc	60
cctatcatan	aaganccttan	caacnttcat	gatccccccc	tcntanncct	tttcctcanc	120
tgcntcctag	tcctgtttgt	cctnttccta	acantcntaa	ganagatnac	taatnctact	180
atctctnacc	tcoggaanct	acaanacgtc	tggaactatt	cngaccccat	gcancncat	240
ntccatcgt	cctccagcc	cctncccttc	ctttacntta	ctnaacgaag	gtcgacgac	300
cctccentac	ctcccnnc	attgggnccc	aanggnactg	gacctcacga	ntacaccnac	360
tacggggnga	ctaagnctgn	aactccttac	atatntcccc	gttaccoccn	gaacncagcg	420
aacngcnaca	ccttggacnt	caagaanta				449

<210> 680

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 680

tttcngtggtg	gtggaattcg	cggccgcgtc	gacgagaaga	nggaggagga	naaggagaag	60
gagaagaagg	agaanaagga	ggagaaggag	aagaaggaga	agaaatcatc	atcatcatca	120
tccactgtct	ngcaactatt	taagtgtgcn	antcccttga	aaacagggtac	ttttgtttca	180
atgtttggga	ccactnctga	cnatgannag	aanaccaata	aatgcttgat	naatgaaaaa	240
nccacttttt	acctgttaga	accctgaggg	taagagaant	gatgtgactc	gacttagtta	300
ccacaaacta	tgatcctagc	atnaattggg	gcctctcaac	acctcaactc	cctgtgcaag	360
aacagatttt	caatgtctac	tgatgatttt	aaatggatta	nttcctctct	ttacttctta	420
agggcatgaa	gntttatgaa	acaaaactat	ncagttccag	acgcttaacc	cacatagtgt	480
taatagtcac	cttcaacaca	cnactaaacc	ccccaaaaan	gntttttacg	gngtttcgac	540
agttttcttt	tctttttgac	ttgnttaaca	cccnngacaa	ctttgtncn	tttccttgaa	600
tcacancttt	cnaanancca	atggtncggg	ttttctctct	tcngggccct	tccttnttn	660
aaaaccanat						670

<210> 681

<211> 494

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(494)

<223> n = A,T,C or G

<400> 681

tcatgggtgc	cacagtctga	tgtgagcgca	ttaaatttaa	ggatctccgc	ccttctcctt	60
aaaactcagg	acttggaat	gancctagga	agcgcccctc	ccctcccan	ccanatccaa	120
gccccggacc	gctgcgnctc	cagctgcgcc	tagtgaaacc	gccgaattcg	aattcacact	180
ggngggccg	gcgaagggtg	gcgcgccgc	gggagcgccg	ggcnagccc	gagggactgc	240
aagccaanaa	nggaggcatg	ggtggcgggg	ggcgccgtct	gatccaggaa	ggagcggagg	300
cgccgatcac	acactcttna	gacgcctgc	ccgcgcctgg	ccagcgcgca	gnctgcagga	360

243

cgcgcgaggc aggaactcgc tggagtttgc caagccccan gnctctggaa agtntgtagc 420
 tccctttcgg ancgnctcct ctggcccttt gggacgggtg tgtcattggg cgggggtctg 480
 tataaggggg ggac 494

<210> 682
 <211> 263
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(263)
 <223> n = A,T,C or G

<400> 682
 tgatcattca agcgntgngc gnataacgat tgctnagccc aacctttcat agggctcgttc 60
 ctttggaat nggatgtcta ttgaatggca gggatagggg cactcggcat tcgcctctgg 120
 tacagttttg catatataat ctcacgcga gcgagcgtag gggancgtta agtttgggga 180
 aatgccnccg catgnccctn ccggagctta aaccccaac aatnccatt ttnaaaaaaag 240
 nttnttant taaaaaaaaa aac 263

<210> 683
 <211> 255
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(255)
 <223> n = A,T,C or G

<400> 683
 cttgccggc atgcacagac ntntttacgg acacnctact ccaagngagc ctgnanctgt 60
 ctacgggtcaa nctctaagg tngncantgc cacanatggc atagtccga gggcggtan 120
 tctggantgc tctctgcact tgaacntaaa gcgcntttca aganaggnet aatngcctgc 180
 ctcttgacaa cnaacaancc cacaccnacc tangaccctn tangcaagga ctggattctg 240
 naaatgcaat acaca 255

<210> 684
 <211> 922
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(922)
 <223> n = A,T,C or G

<400> 684
 acccttcatt tcatgtgott ctattttcct acatctttta catgactaag ggattaatga 60
 aatcacctot tcataatcat gaccataatt tcatacaaca agtactcaag tttgggtgta 120
 gcactttatt aatgcttacg aattctctct ctctccctct ttctcttttc cttagtcctt 180
 gcacaataag gatttttgaa tgtataatat catcttaggt aagctttcat atggtttttg 240
 catatgaagc ttatgactgt cataagccat accaagcctg tggagtatgg catgattttc 300
 attacataat ccaatgaaaa tagacttatt ttaaatccct aactttgtag ttttaatttg 360
 tatttcacta tcttgaaatt aacagctagt acttatccat cacagcagtc tcctactgac 420
 atgaagcaag ttgttgaatg cagtaganca tgaatgaaag catttaatgt tanacaaaaa 480
 tgggtgatac ccaagcattc tgaattattt gcatcaagga atgggacatg tacattagt 540

244

```

gcatcatttc taccaatatg tgacttgaat tgttttttta aaaaaaggan aatgantttc 600
tcaatttgct ttaaaaaatt ttnaaaaagt tcaatggcat gctgctttgt ctggacttaa 660
tttattaaca attnttaanc cttccttaag gacanaattt tgggtgttcag gatcnccttg 720
aagggtctta tttttnatan nattccaaac ccaaaaagggtg gtttaaaatg ggnggggttcc 780
ccccncnaaa atttgaccg gcttttttat atttaaaaaa nttncnttt gngtttgaaa 840
nctnaatacc aattaagggg gaattttacc tnccagtggg aaaaaaaac nctngccntt 900
naaaaaattc ccnggagnca at 922

```

<210> 685

<211> 531

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(531)

<223> n = A,T,C or G

<400> 685

```

tgaggctctg taaaactggt cctctgctag gcatacttca tattctctat attaaactca 60
tctttaattg gcattggaaga ttcatgttgc caaatctcag atgaagatcc tatattggat 120
gcaattaagc ctggcagcgc cctcaaaaga cagtcttgct actgctagcc acagccagga 180
cacagtaaca gtctcttcta gtgaccnag accataanaa atananatct aaagaattct 240
gactccaaag gcattagccc attcctggta ttgccaatga tgatagaaaa aattgccaaag 300
ctcctgggac atggaaatac actcagtaca tttgagaact ggagaactan tttccaaaat 360
agtatgaaga catganggtg attgtagata tntgagtttg gagaanttga gggaaatcng 420
attacacatg tttactacaa gagatgttna taagtaaaga aggcctgata tacaatctaa 480
cagacnantg agataaatct taantcacia ctgaontccc ttttggggcg g 531

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<210> 686

<211> 336

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(336)

<223> n = A,T,C or G

<400> 686

```

ggngncctna tgagcgcgcg taatacgatc atatagggcg aattgggtac cgggcccccc 60
tcaagaacac tacaagctat gtctcttct canagagccc tgaantttta acatattgaa 120
agctctnatc ttgccaaana actccactta acttcaaaac acaccctcca cacacatcat 180
gatcaactna gatcttactg aaccagaatc ctnaatggca tacttcagga acaggggtcc 240
anagaagcag ttctcaaant gcagctnaaa aagaaactga aaaccaat catgcaanac 300
ctagggctta tttgagagca ttttcagtg cagatt 336

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<210> 687

<211> 271

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(271)

<223> n = A,T,C or G

<400> 687

245

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aatctgcact ggaaaatgct ctaaaataag ccctaggtct tgcatgaatt gggttttcag      60
tttcttttta agctgcactt tgagaactgc ttctctggac ccctgttcct gaagtatgcc      120
athtagatt ctgggtcagt aagatctcag ttaatcatga tgtgtgtgga ggggtgtgtt      180
tgaagttnag tggagttctt tggcaagatc agagctttca atatgttnaa acttcagggc      240
tctctgagaa gaggacatag cttgtagtgt t          271

```

<210> 688

<211> 740

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(740)

<223> n = A,T,C or G

<400> 688

```

tgatgaagcg cgcgtnttac nactcactat nggggcgaan tatgggtacc gggnccccct      60
cgaagcggcc gccctttttt tntttttttg tgagagtta aataaaatat ttgagtttaa      120
tttaaagttt gagtttaatt aaaatatatg gcataatcca agttgggctt tgcanaaaga      180
acacttctca ggaactgtta gttgggtgtac caggaactca gaagggtcct gttattaaat      240
atatttgga aatgcatgga ttctctgaan atcnctctgc atgtgagcaa cacttacatc      300
ncaaaccaaa attggcattg catacatnaa ccaatatttc ccaaacattt ctggttatgg      360
cccacccctt ttgtgtanta cttattgtctg ttttttgga ccctggggaa attacttaaa      420
atattcagct ggaaattaca ggcgttactt ttaaggganc aagaattaca gtgactccca      480
aaattgcaag tgttgattac tatttaagaa cccaagaatt tgaaagaaat tttgaaaagt      540
gaaaacngga aatnttaaat gacttctcaa attttgaaaa ctcnngnaaa catctccact      600
ttggtncctt tccttttaaaa attggctaaa aattntttnt tatnccacc ccattggaan      660
tncccccccc ctggaacaat tggattcccc tatttcttaa aaaacggccn cccccccggg      720
ggngaacncc nacnttttgn          740

```

<210> 689

<211> 635

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(635)

<223> n = A,T,C or G

<400> 689

```

actagtccag tgtgggtgga ttccattgtg ttgggattac atatactttt agcaattttt      60
aaagaagtgt acaaagttga gatgtttcct gagctctcat atatctgana atgtcatttt      120
acatctccgt cttcacctct caaaacttct ttcaattctt tggctcttaa tagtaatcaa      180
cacttgcact ctggagtcac tgtaattctt gtccttttac agctacnctt gttatttcca      240
gctgaatatt tttagttatt tcccagggtt ccaaaaaaca gcaataagta ctacacaaag      300
gggggtggcc ataaccagaa atgtttggga aatactggct catgtatgca atgccaaatc      360
tggtttgcna ttgtantgtt gotcacatgc agagtgaatc ttcaaanaat ccatgcattt      420
tccaaatata ttttaataaca gggaaccttc tganttcttg gntacaccaa ctaacagttc      480
ctgaaaaatg ttctttctgc aaaacccaac ttggggatat gccatatatt ttaattaaac      540
tcaaacttta aattaaactn caattatttt attttaaaact cctcaaaaaa aaaaaaaaaa      600
agggggggcc cttccaangg ggggnccggt tcccc          635

```

<210> 690

<211> 3923

<212> DNA

<213> Homo sapien

<400> 690

acagaagaaa	tagcaagtgc	cgagaagctg	gcatcagaaa	aacagagggg	agattttgtgt	60
ggctgcagcc	gagggagacc	aggaagatct	gcatggtggg	aaggacctga	tgatacagag	120
gaattacaac	acataactt	agtgtttcaa	tgaacaccaa	gataaataag	tgaagagcta	180
gtccgctgtg	agtctcctca	gtgacacagc	gctggatcac	catcgacggc	actttctgag	240
tactcagtgc	agcaaagaaa	gactacagac	atctcaatgg	caggggtgag	aaataagaaa	300
ggctgctgac	tttaccatct	gaggccacac	atctgctgaa	atggagataa	ttaacatcac	360
tagaaacagc	aagatgacaa	tataatgtct	aagtagtgac	atgtttttgc	acatttccag	420
cccctttaaa	tatccacaca	cacaggaagc	acaaaaggaa	gcacagagat	ccctggggaga	480
aatgcccggc	cgccatcttg	ggtcatcgat	gagcctcgcc	ctgtgcctgg	tcccgtttgt	540
gagggaaagg	cattagaaaa	tgaattgatg	tgttccttaa	aggatgggca	ggaaaacaga	600
tctgtgtgtg	gatatttatt	tgaacgggat	tacagatttg	aaatgaagtc	acaaagtgag	660
cattaccaat	gagaggaaaa	cagacgagaa	aatcttgatg	gcttcacaag	acatgcaaca	720
aacaaaatgg	aatactgtga	tgacatgagg	cagccaagct	ggggaggaga	taaccacggg	780
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cccaacattc	tccatatatc	cagccacact	catttttaat	atttagttcc	cagatctgta	960
ctgtgacctt	tctacactgt	agaataacat	tactcatttt	gttcaaagac	ccttcgtgtt	1020
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gctttagaat	tttggcaaat	catactggtc	acttatctca	actttgagat	gtgtttgtcc	1980
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gacacatatt	agcttctagc	ctttgcttcc	acgactttta	tcttttctcc	aacacatcgc	2940
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caagaggttc	aaaatccaac	tcattatctt	ctctttcttt	cacctccctg	ctcctctccc	3180
tattattactg	attgactga	acagcatggt	ccccaatgta	gcatgcaaaa	tgagaaaccc	3240
agtggctcct	tgtgtgacat	gcatgcaaga	ctgctgaagc	cagaaggatg	actgattacg	3300
cctcatgggt	ggaggggacc	actcctgggc	cttcgtgatt	gtcaggagca	agacctgaga	3360

247

```

tgctccctgc cttcagtgtc ctctgcatct cccctttcta atgaagatoc atagaatttg 3420
ctacatttga gaattccaat taggaactca catgttttat ctgccctatc aattttttaa 3480
acttgctgaa aattaagttt ttctaaaatc tgtccttgta aattactttt tcttacagtg 3540
tcttggcata ctatatcaac tttgattctt tgttacaaact tttcttactc ttttatcacc 3600
aaagtgggctt ttattctctt tattattatt attttctttt actactatat tacgttggtta 3660
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tacctaatac atgtgggact taaaacctag atgatgggtt gataggtgca gcaaaccact 3840
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aagtaaaatt taaaaaaaag tga 3923

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<210> 691
 <211> 882
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(882)
 <223> n = A,T,C or G

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<400> 691
ttactcacta tagggctoga gcggccgctg aattctgctg cagtgaagctg tgattatgtc 60
cctgcactcc agcctggatg acagaacacg atcatttctc taaagacaaa caaaaaacat 120
aaaataaaac tagtataagg atagaagccc aggggttgatt taagtctgcg gaaatcataa 180
accataggtc agacttctca ttgatgaggt acttggtggg tagaatacaa ttaggtatat 240
ttggtctaga aaccaggatg gaattagaga ataaaagact gagcaatagc atgtttagt 300
attagaaata ctatagaaat aggaaaagcc ctgattatga ctttggagtt ctgatccaac 360
atctgggatt atttagatat tttaaaggaa aacgatgact tttagctctc aggatgttag 420
tttctcaaac cataaaatga agagcctcga aaagatttgc tttaccagat ttttctgaa 480
gtcaattcca gttctaaaat tccatcactg ngcactaagg caaattgaat tgaataaagt 540
attgggnatg cataaaatac tctattttta aaaangaata gtaattatcc attggnaaac 600
gacgcantca tccagnatc tctaccctg nccatgncn tatgtagana tgtantctca 660
atcccttaac aaaccgattt tgcaaaaggag cttanccttg gggtaacttg tcanggcaac 720
tggtctactt tnaagactca tcttcaacta ctgggcacca aatncctacc attgcatcaa 780
actgggggtc ccatncaagg caaaccctgn gaaatcttta atcccgaat tggcgcccac 840
ttttgngggg tttccnaaaa gaatcntccc ccccgagggg cc 882

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<210> 692
 <211> 235
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(235)
 <223> n = A,T,C or G

```

<400> 692
ccgcactngt aangnccgcc agnngctgn aantccgctn agcncggatc cactagtcca 60
ttgatggtaa aagggtagct tactggnatg tccgntgct ccanganata atacncagga 120
cttctcanag cacttaatat gttaataata aactncngga aaaaagatnt tcnatgaanc 180
nttctcttta ggaggtcagg ngagaatagt gttaatgnca ttaagganag aacga 235

```

<210> 693
 <211> 383
 <212> DNA
 <213> Homo sapien

248

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

<400> 693
nttatgtaag aaatgtcata tatcttttat tttcttttaa tcaaaataaa tatgactttg 60
agcatcccat cccatgcccc atcctatcag aatggtagga acatcaacac aaataattag 120
taatgcaccg catctacatt cccatgctct ctttacttct tcagcattgc cttaaaggcat 180
aatacacctt taattaatta attcagcctc ctaatgcaca ttaacaaagc ccttgctaga 240
ctctgtccat aatggnaaac ctgnatgac cttgatatta acantttaag gaatgctcat 300
ggattggtn cagacttaaa aaattgaggg ggctgaanaa aatctaangg anaaatcatg 360
gaagcatttg cacatattac ata 383

<210> 694
<211> 204
<212> DNA
<213> Homo sapien

<400> 694
tctcttggtt ggctcagcctg aagggtggta atgactcacc aacgctacta atccttcttc 60
actgtccctt atttttttcc ctcccaggct cataactcga ggttaaactc tcttttatac 120
aagaaccctg tctgatgaag catcatttca gaattttaag tcaacttaca aatgtggtat 180
tattcacatc tgagtacaaa tttta 204

<210> 695
<211> 670
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(670)
<223> n = A,T,C or G

<400> 695
gcaccagccc aggtgctggt tcttcaacttg agctccatga ccctccctgt gtggtggggt 60
gaacggtgac ctccaaaaga tatgtccacc tggaacctca gaataagatc ttatttggaa 120
tagtctttgt agatgtcagt aaggtaaaga tttggagatg agaccctcct ggattaggg 180
aggccctagg tccactggca ggtgtgcttc tcagggtctg aaaggggaag acagggccac 240
ccagaggagg agacggaggc agagacagg ccaccagag gaggagacgg aggcagagac 300
agggccaccc agaggaggag acggaggcag agacaggggc caccanagg aggcagagga 360
ggcagagaca gggccaccca gaggaggaga cggaggcaga gacagggcca cccaaaggag 420
gagacggagg cagaanacag gccccccaa agaaganacc ggaggcanaa aacagggcca 480
ccanaggagg gagacggagg canaaacagg gccaccccaa aggaggagac ggaggcaaaa 540
cagggccacc caaaaggagg aagccggaag gaaaaaacag ggcccccca aaggaggaag 600
ncggagggcn aaaaanaggg cccccccaa agngagaaaa ccnggnaggc nanaaaaccn 660
ggggcccnnc 670

<210> 696
<211> 317
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(317)

249

<223> n = A,T,C or G

<400> 696

tgacccgttn	tttctgcaaa	ggagagtggg	gaaggagggn	tggaagaca	aaagttacat	60
gttagcaggg	aagagaacag	aattttatcc	accottatct	ctttagttag	tgaacaaaca	120
gcccactgtc	atcgtaggata	catttcactt	ttttocacatg	actaaggagc	tctccggagt	180
gaagagttag	taaataatgtt	tattacgcat	tcatttgcta	agaatcatca	agaacccaaa	240
gttagagacg	tttcgtgggt	gaactttctc	cctactgtct	agtagaatta	tatggggatt	300
ctggatctgc	tggtgcc					317

<210> 697

<211> 246

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(246)

<223> n = A,T,C or G

<400> 697

ctncagctct	aatcgactnc	tatnaggnat	gatggcncgt	gcngcgcgta	cgtantgctt	60
ggatcctcnn	anagcggacg	cctactacta	ctaaattcgc	ggncgcgttg	actttttttg	120
tttttttct	tnacagagnt	ntttttgtgc	ccttggttct	tatgctcana	ctcngcaaaa	180
aanatcaaaa	gntacnntg	aaaaacntat	nccatctnca	naaaggaggt	gnagntatta	240
ctttct						246

<210> 698

<211> 3674

<212> DNA

<213> Homo sapien

<400> 698

agaaagtttc	cttttttttt	tttaatgggtg	aaaagatata	cacatattta	gaattagcca	60
gctgggctca	gttttagatta	ttccaatttt	gttggaaca	tccagagcat	cgtaatcagg	120
agccagtga	acataattcct	tcttctctcc	atcaggccaa	atcacgggtg	tgaccttggc	180
cacatcaatg	tcttagaact	tcttcacagc	ctggttgatc	tggtgcttgt	tggtcttaac	240
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<210> 699

<211> 2051

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(2051)

<223> n = A,T,C or G

<400> 699

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251

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<210> 700

<211> 2841

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(2841)

<223> n = A,T,C or G

<400> 700

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<210> 701

<211> 3228

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(3228)

<223> n = A,T,C or G

<400> 701

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<210> 702

<211> 4894

<212> DNA

<213> Homo sapiens

<400> 702

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<212> DNA

<213> Homo sapiens

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<212> DNA

<213> Homo sapiens

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259

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<210> 706

<211> 123

<212> PRT

<213> Homo sapiens

<400> 706

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Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val
      20              25              30
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
      35              40              45
Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly
      50              55              60
Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu
      65              70              75
Tyr His Arg Glu Lys Gln Val Leu Ile Gly Gln Trp Val Glu Ser Gly
      85              90              95
Trp Glu Gly Trp Ser Gly Phe Leu Gly Gly Gln Leu Ala Gln Asn Leu
      100             105             110

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260

Val Ser Gly Lys Gln Leu Trp Arg Met Leu Leu
 115 120

<210> 707
 <211> 150
 <212> PRT
 <213> Homo sapiens

<400> 707
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 20 25 30
 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val
 35 40 45
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Glu Ser Leu His Pro Pro
 50 55 60
 Ser Phe Leu Phe Gln Ile His Ala Thr Trp His Val Gly Gln Glu Tyr
 65 70 75 80
 Leu Cys Pro Gly Ser Cys Leu Glu Gly Glu Val Val Cys Trp Glu Gly
 85 90 95
 Ile Ala Gly Gln Glu Gly Asp Pro Gly Leu Arg Gly His Thr Lys Arg
 100 105 110
 Lys Lys Arg Ile Pro Arg Thr Tyr Pro Ser His Leu Trp Ile Pro Gly
 115 120 125
 Pro Ala Gln Ser Leu Ala His Arg Arg His Trp Arg Asn Ala Pro Asn
 130 135 140
 Leu Trp Leu Ala Leu Leu
 145 150

<210> 708
 <211> 371
 <212> PRT
 <213> Homo sapiens

<400> 708
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 20 25 30
 Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
 35 40 45
 Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
 50 55 60
 Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
 65 70 75 80
 Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
 85 90 95
 Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val
 100 105 110
 Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro
 115 120 125
 Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
 130 135 140
 Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser
 145 150 155 160
 Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu
 165 170 175

261

Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala
 180 185 190
 Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala
 195 200 205
 Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe
 210 215 220
 Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys Cys Arg
 225 230 235 240
 Met Pro Arg Thr Leu Arg Arg Leu Phe Val Ala Glu Leu Cys Ser Trp
 245 250 255
 Met Ala Leu Met Thr Phe Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu
 260 265 270
 Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg
 275 280 285
 Arg His Tyr Asp Glu Gly Lys Ala Leu Ala Ala Ser Arg Gly Trp Cys
 290 295 300
 Gly Ser Arg Pro Pro Glu Thr Thr Leu Gly Ala Val Ser Gly Leu Val
 305 310 315 320
 Pro Leu His Pro Gly Pro Asp Phe Ser Val Arg Lys Val Gly Met Asp
 325 330 335
 Pro Ile Cys Ile His Gly Phe Ser Trp Val Trp Asn Ile Ser Ala Cys
 340 345 350
 Gly Phe Arg Lys Ala Ser Gly Cys Ser Arg Ser Leu Ile Arg Val Val
 355 360 365
 Ala Pro Val
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 <222> (1)...(141)
 <223> n=A,T,C or G

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 taacnaance cttccccctt t 141

<210> 710
 <211> 196
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(196)
 <223> n=A,T,C or G

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 ccttancaat nggtttttn tttttgtcc ctnggnccgn gcgattcaan aaattgaagg 180
 cccanaaaaa ccccct 196

262

<210> 711
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<212> DNA
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<220>
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<222> (1)...(177)
<223> n=A,T,C or G

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ttcnacaata ctgctatcct anttnttctn tcncctctct cccannttac taaccac 177

<210> 712
<211> 185
<212> DNA
<213> Homo sapiens

<220>
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<222> (1)...(185)
<223> n=A,T,C or G

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ctgggttgcc gtgtgcgacg ganggccacg tccctctgnc ntgagtanca catagcatcc 120
acgttttagtc gactntnccg ggcggccgct ctaccctnt atngattctt attaaaantc 180
ggatc 185

<210> 713
<211> 172
<212> DNA
<213> Homo sapiens

<220>
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<222> (1)...(172)
<223> n=A,T,C or G

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cactacacgg cncctnccg agccnnggtc agtgccctnct nggagacctt ctctggggca 120
ggangagcac tnggtatggt cacgtatcnc ttcntaaana tacnnccctc cg 172

<210> 714
<211> 112
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(714)
<223> n=A,T,C or G

<400> 714
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263

ctcactatnc ggcancgcag gcgcagcagg gaanggggtca cctcccagtc tc 112

<210> 715

<211> 326

<212> DNA

<213> Homo sapiens

<220>

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<222> (1)...(326)

<223> n=A,T,C or G

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gttctncaac gttcctgact nggaancccc ngcngttcng atccnonggt acctagctcc 180
anntcccccg tntccttct ggngtntcat naangaggac cncctcgcg cnccttcct 240
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<210> 716

<211> 122

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(122)

<223> n=A,T,C or G

<400> 716

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<210> 717

<211> 203

<212> DNA

<213> Homo sapiens

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<223> n=A,T,C or G

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ngntggacca ngttggtttt ctgctgtgtg tgtggcagta gtaagttatt agtttttana 180
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<210> 718

<211> 168

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

264

<222> (1)...(168)
 <223> n=A,T,C or G

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<210> 719
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 <212> DNA
 <213> Homo sapiens

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 <222> (1)...(210)
 <223> n=A,T,C or G

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 aganatntcg gncgcttcat tantcatcct tcttaccan ntctctngat ncnagnttg 180
 ancntgaacg cacactacng gatntctcca 210

<210> 720
 <211> 131
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(131)
 <223> n=A,T,C or G

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 gaagcaccct t 131

<210> 721
 <211> 121
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(121)
 <223> n=A,T,C or G

<400> 721
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 a 121

<210> 722
 <211> 246
 <212> DNA
 <213> Homo sapiens

265

<220>
<221> misc_feature
<222> (1)...(246)
<223> n=A,T,C or G

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gnttcntcga tatgaanaac actaatccca tgtngtntgn gtctccgtga ttcattccctc 120
gcacnggtcc cnttcnaac cnttgcatag gtgttatgtt gtantctccc cagtgcacaa 180
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atcaag 246

<210> 723
<211> 160
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(160)
<223> n=A,T,C or G

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gnatcnanta gccgtncctg ananccaacg cccctacgtc 160

<210> 724
<211> 156
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(156)
<223> n=A,T,C or G

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gagcctttcc actttttctac taataaaaaa atgcaccagc cctaccann agtgnggaaa 120
acctccttag gcccttgnnt ggaacaancg aaaatc 156

<210> 725
<211> 347
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(347)
<223> n=A,T,C or G

<400> 725
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gagcccgccg ncagacgccc catcagtagc gtccgcaccg ggnagccgcg gntctcgccc 180
gagccgtggg cgcgcccag gagcgggctc gcctcccgcc gtccctcgca gctctgccg 240

266

gccccagccc ggcgcgtcgc cgccgccgnc ttgccgctcg gncgcgcggg nccggnaaac 300
gcggtcgagg tctggatgng gcanngcccg cncctntcgc tgagcct 347

<210> 726
<211> 162
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(162)
<223> n=A,T,C or G

<400> 726
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tcccgccctt tnggtnccca aaganacnaa gggggagtcc cttnatagag gnagncgat 120
nntcncaac nactngact ttgnccatgg ggagnaaggt gg 162

<210> 727
<211> 120
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(120)
<223> n=A,T,C or G

<400> 727
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ggggtcnctt anagngnagg ggttctctcc ccaccacttg ncttgnccat tngagnaag 120

<210> 728
<211> 130
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
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<223> n=A,T,C or G

<400> 728
gaccactgc agcgttnaac ttagcttggg ccgagctcgg atccctagtc cgtgtggtgg 60
aattccatgt gtcgagagag gggcaaatac nctccaanac ancncctca tgctcnacac 120
atattcgat 130

<210> 729
<211> 182
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(182)
<223> n=A,T,C or G

<400> 729

267

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cngactgctn gcgttttaaac ttaagcnagg taccgaacgg ggatnnacga ctantgatcg 60
gctggctgct tccagtcgat tanatttggt aaaaagctga accncngccn gttaaggggg 120
annatgcaaa ananctatcc nnctgccccn taaactgntc tntccnaggg aaaaaangga 180
ag 182

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<210> 730
<211> 678
<212> DNA
<213> Homo sapiens

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<220>
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<222> (1)...(678)
<223> n=A,T,C or G

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ttggaagga aatncccc 678

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<210> 731
<211> 135
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (1)...(135)
<223> n=A,T,C or G

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<400> 731
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gatccgagct aagcc 135

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<210> 732
<211> 660
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (1)...(660)
<223> n=A,T,C or G

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<400> 732
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tgaaaataaa gaaaaaaaaa tgaagctgcc tatcaagttt tggattatc aaaaacttcc 180

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268

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tacaagttat tttacttcaa ccatgttatt acaaatatatt taatgaatac ttttagagact 240
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ttgataatta cataaattat tatggtccat tcaacttttc tagtgtttag tttatacacc 360
aggaagactt tcctattcta ctaacattta taaagtatgc taacctatta tttaaacgca 420
tccactatta ggattttatg gcctaaaacg tgatacagtt cagtatcttg atgtcaaaac 480
tttttaagca agtagggatt aagttcaagt gaatgtgatt ttctttcttc ccagtagggg 540
cttctgaata actcagnaac gctcacttcc attatcttac tttataaaaa aatgctataa 600
gacagaatgg gccgacgtgg nggctccacc tgtatccacc tttggaggcg agnggcgaat 660

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<210> 733

<211> 836

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(836)

<223> n=A,T,C or G

<400> 733

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tagctactca ttttctgggc cacgaagggt cctaaaatgg gaagaagtgg agatctgacc 120
ttgttagttc taaatacact aaactgggag tgccatggat ggctttcagg atgtcctgaa 180
tcctctataa ttgtatacaa aatcgtgagt ttttaaaaac tgggttagag ctattgggtc 240
ctcagagtct caggcatctt agaccccaa aaagggttaag gactactgac ttaaccaatt 300
aggtttgagt ggcattggct ttgaagaaa gcagaggaaa gatataattt ataattctgg 360
gcaacaaaaa agtggatgtg tgccagcatc ttagagtaga atcctcttaa aaggatagca 420
ctgcatatga actagtaggt ttaaccagt gcatatttag gcgaagtagc tcatttttct 480
gttagaattc ttttttattt gggaatgggc aagcttttac agcttttacc ttgccaatga 540
atacctggaa tttaaaaaat ctgtgtaggc atattgcccc taaagttttt tttcctagat 600
catatattca gtaaatatgt ttgtagcttt atttcaatcc cccaattcat tgagggttga 660
aacaatttga atggtttgag tgtagaagct aagttatttc tgtagaggct aagggcattt 720
ataccaanat atgttagact tngngntcct gtaaccatg ctgtanacaa taggaattac 780
tgtatatcca cattttaatt ttaacatctt ctgctttgnt gntgggttga gangga 836

```

<210> 734

<211> 694

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(694)

<223> n=A,T,C or G

<400> 734

```

nagtnctatt tncactaaac tngnagtgcc ttggatggct ttcaggatgt cctgaatcct 60
ctataattgt atacaaaatc gtgagttttt aaaaactggg ttagagctat tggttcctca 120
gagtctcagg catcttagac ccccaaaaag gttaaggact actgacttaa ccaattagg 180
ttgagtggca ttggctttga agaaaagcag aggaaagata tattttataa ttctgggcaa 240
caaaaaagtg gatgtgtgcc agcatcttag agtagaatcc tcttaaaagg atagcactgc 300
atatgaacta gtaggtttta accagtgcac atttaggcga agtagctcat ttttctgtta 360
gaattctttt ttatttggga atgggcaagc ttttacagct tttaccttgc caatgaatac 420
ctggaattta aaaaatcttg ttaggcataat tgcccataaa gtttttttct ctagatcata 480
tattcagtaa atatgtttgt agcttttatt caatcccca attcattgag ggttgaaaca 540
atttgaatgg tttgagtgtg gaagctaagt tatttctgta gaggctaagg gcatttatac 600
caagatatgt tagacttgtg gttcctgtta accattgctg tagacaatag gaattactgt 660
atatccacat ttttaatttt aacatcattc tgctc 694

```

269

<210> 735
<211> 126
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(126)
<223> n=A,T,C or G

<400> 735
ncnttgaaac nggttgacca gacttcaggc ctgtgcgctc aatcgtggag aatctcgtgc 60
cgaattcggc acgagtctct ctctctctct ctctctctct ctctctctct ntctctctct 120
ctctct 126

<210> 736
<211> 165
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(165)
<223> n=A,T,C or G

<400> 736
cagaagcctt taaaccggtt ngaccagact tcaggcctgt gcgctcaatc gtggagaatc 60
tcgtgccgaa ttcggcacga gtctctctct ctctctctct ctctctctct ctctctctct 120
ctctctctct ctctctctct ctctctctct ctctctctct ctctc 165

<210> 737
<211> 125
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(125)
<223> n=A,T,C or G

<400> 737
ggnagccctt ttaaccgttt gtccagactt caggcctgtg cgctcaatcg tggagaatct 60
cgtgccgaat tcggcacgag tctctctctc tctctctctc tctctctctc tctctntctc 120
tctct 125

<210> 738
<211> 137
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(137)
<223> n=A,T,C or G

<400> 738

270

```

ggagnncnctt gancaggatg accgacttca ggcctgtgcg ctcaatcgtg gagaatctcg 60
tgccgaattc ggcacgagtc tctctctctc tctctctctc tctctctctc tctctctctc 120
tctctctctc tctctctc                                     137

```

```

<210> 739
<211> 970
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(970)
<223> n=A,T,C or G

```

```

<400> 739
aggcctatatt aggtgacact atagaacaag tttgtacaaa aaagcagggt ggtaccgggtc 60
cggaattcgc gccgcgctcg acggcccttn gtgccactag ntctttcatt cttccccccc 120
atcaatcagt gaacttttta gcctactcaa agctttgtct caatgcatag gatttatgat 180
tgtggggatt tccagataat ataaatattc aacatgaata ttttaaatta aggcatagaga 240
catttttctt aactgagcat agccatgaac ctctcacgtc tgttcctctg tgtcagtttg 300
tancactgaa tacagcagcc ctccataaaag tccaggcagt gcacagggtc tgacatgatg 360
aagtgcgctg ttgctatggt gattttgcag ctggccaaat agtcactggt tgattttacc 420
cagcaggaga tttttgcaaa aatttcctgg gtgagagtga aatcaaactc ctattttgnt 480
tctcctctgc aagctgnagt taagatggat taatgagtag ttttagatta attaactctg 540
aagagaaaaa gggagaaaaa tgaggaaagt tgttggcaga agtcattgct ggaatccttc 600
tgaagggagt actgacttca cttgcaaaga cnagagacta naagacaatg aagttaaact 660
tggcctgtct ctcatatgat agatgctgag agtcaggntc agggaaattt aattctgtca 720
tagcatatnn gatttatgtg gtcattggatt tgttggcact aaccngcctn taatcagnat 780
aagaaaagtg ttttggtaga naaagaaaaa tatggcccag aaaaacctgg aanacttgga 840
aaaaatgntn gggggccttg ggtggtggtc tnaaaanacc ccctggggat ntttaaacca 900
aaantgaaga agggaaaaat ntttccccnt nttttntttt tttgccccct tgggattggn 960
ttttntttcc                                           970

```

```

<210> 740
<211> 739
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(739)
<223> n=A,T,C or G

```

```

<400> 740
gntgtcnaaa aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cggcccttgg 60
tgccactagt tctttcattc ttccccncca tcaatcagtg aacttttttag cctactcaaa 120
gctttgctcc aatgcatagg atttatgatt gtgggggattt ccagataata taaatattca 180
acatgaatat tttaaattaa ggcagtagac atttttccta actgagcata gccatgaacc 240
tctcagctct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgtagc 360
tgcccaaata gtcactggtt gatttttacc agcaggagat ttttgcaaaa atttcctggg 420
tgagagtga atcaaactcc tattttggtt ctccctctgca agctgnagtt aanatggatt 480
aatgagtact ttttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
gttggcagaa gtcattgctg gaatccttct gaagggagta ctgacttcac ttgcaaagac 600
aagagactan aagacaatga agttaaactt ggcctgtctn tcatatgata gatgcttgag 660
agtacaggnt cagggaat ttaattctgn catacgcata ttggattatg tgggtcatgg 720
ctttgtttgg cncctaacc                                           739

```

271

<210> 741
 <211> 1171
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(1171)
 <223> n=A,T,C or G

<400> 741.
 gccttgnggt gacactatag aacatgtttg tacaaaaaag caggctggta ccggtccgga 60
 attcgcgggc gcgtcgacgg cccttnntgc cactagtctt ttcatctctc ccccccacatca 120
 atcagtgaac ttttttagcct actcaaagct ttgctccaat gcataggatt tatgattgtg 180
 gggatttcca gataatataa atattcaaca tgaatatatt aaattaaggc atgagacatt 240
 tttcctaact gagcatagcc atgaacctct cacgtctgtt cctctgtgtc agtttgtagc 300
 actgaatata gcagccctcc taaaagtcca ggcagtgcac aggtcttgac atgatgaagt 360
 gacgtgttgc tatggtgatt ttgcagctgg ccaaatagtc actggttgat tttaccacgc 420
 aggagatttt tgcaaaaatt tcctgggtga gagtgaatc aaactcctat tttgtttctc 480
 ctctgcaagc tgtagttaag aagggtatga tggagtactt tttagaatt aaattaacct 540
 cttgaaagaa gaaaaaatgg gggaagaaaa aaagtgaag ggaaaaggn ttggttttgg 600
 gccnaaaaaa aagttccaan tttnngcctt ggggaaaaat tccccntttt ccttggnaaa 660
 aggggggnaa ggttaancct tgggaacctt tttccnncct tttnngccca aaaggggaac 720
 ccanggggaa agaaccttta ggnaaaggaa acccatttgg gaanggggtt naaaacctt 780
 ngggcccccg ggcctcctc caanaaggga aaaaaaagg cctggaaaan gtaccagggt 840
 ttcangggna aaanttaaaa ttcttggcca atancccat aattgggaat tatggggggg 900
 ccatgggctt ttggttttgg cncctaaccc cgcnttttaa attcaanna aaaaaagng 960
 gtttggaaaa nnaaaanaaaa aaaattnaan ggnccnnaaa aaaaacctg gaaaacctt 1020
 ggaaaaaaat tngnngggg gccnttttgt tgggggggt tnaaaaaacc ccctngggg 1080
 ttttttaagc ccaaaaggg gggaggggna aaanggtnc cttntttttt ttttnngccc 1140
 cccttgggga atggnntant tcanggggccc c 1171

<210> 742
 <211> 739
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(739)
 <223> n=A,T,C or G

<400> 742
 gntgtcnaaa aagcaggctg gtaccggctc ggaattcgcg gcgcgctcga cggcccttgg 60
 tgccactagt tctttcattc ttcccncca tcaatcagt aactttttag cctactcaaa 120
 gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180
 acatgaatat tttaaattaa ggcataagac atttttccta actgagcata gccatgaacc 240
 tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tctaaaagt 300
 ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgcagc 360
 tggccaaata gtcactggtt gattttaccc agcaggagat ttttgcaaaa atttcctggg 420
 tgagagtga atcaaaactc tattttgttt ctctctgca agctgnagt aaataggatt 480
 aatgagtact ttttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaaggtt 540
 gttggcagaa gtcattgctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600
 aagagactan aagacaatga agttaactt ggcctgtctn tcatatgata gatgcttgag 660
 agtacaggnt cagggaattt ttaattctgn catacgcata ttggattatg tgggtcatgg 720
 ctttgtttgg cncctaacc 739

272

<210> 743
<211> 610
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(610)
<223> n=A,T,C or G

<400> 743
ctgtccttat ttcttttagca aaaatttccc aagagaagaa ttgctgggat aatgcacatt 60
taaatttttg atagacattc ccaaataatta tacctgtttt tgagaccttt aattcctgtt 120
gtcaaattgc cctatatatg gagtaataaa cacgatttaa agaaatgagg actaaaaaaaa 180
gattatatat aacccaacat aaaggcaacc tcttaggcgt tgacagaaac tgacaacttt 240
ttatctgtgg gtgcgatcca ttataagtaa cctgagcacc ttattttttc tttttaaact 300
ctaggtagga taccogaggt ccacaattt ttcataagaa atattttttc tctgccctat 360
gagattttta aaaatattat actgcttcaa ttgcatcaaa agaaatggac cctaatatct 420
atgatgaagg atttggaggt agaagacctg agtttcaatt ttggcatggc tgtttgtcta 480
gctctgngat cttggacagg tcaattgact tggcttaatc ttctcatcca tttagnngag 540
acagcaccac tattcacagg actattgncn gaattaccag acaatagcat agngaaaaat 600
ataangcctt 610

<210> 744
<211> 127
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(127)
<223> n=A,T,C or G

<400> 744
ttnacctccc tggaccgggc ccccttccc cgggcggnct ccccgggctg caggaattct 60
gcacgaggga gagagagttt gagagagaga gagagagaga gagagagaga gagananaga 120
gagagag 127

<210> 745
<211> 458
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(458)
<223> n=A,T,C or G

<400> 745
gatatcccgg gattcgcggc cgcgtcgacg tggcctctag tttgtcctgg tccaaagcag 60
ggaagctggg ctacgtcctg cccaggctcag ccttaggtta agggctgcct gggggaggga 120
acttctctgg ccttcgggtc tctgtgcact ggggtggctc ctgtggcca gaatgccctg 180
gagaaggggt ctaactggaag cgaagggtga gggcagcagg gcctgaggcg caggagctgg 240
tgagggtcc cagcacaggt cgccgcccc gtcacatcac tgctgatggt ggggggactt 300
ggggagtttc ccccgagaat gggagggtctc acagtccccg tgctgcaatg ctgtcgggtc 360
actgngncng caatgtgctc atggnacatt gctttttctc tgtggccccg gccgatttat 420
ccagcanngc acccctcttc tncctctccg anaaagcc 458

273

<210> 746
 <211> 893
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(893)
 <223> n=A,T,C or G

<400> 746
 aagcaggctg gtaccggtcc ggaattcgcg gccgcgtcga cgtggggagt tagctctctg 60
 gaccccgctca tagagtaagt catcgataga gcatttgctt gatggggact tccagaaggc 120
 canngaaagt cctgccgact tcctggggaa gcccatccgc acgtgggggtg aggggtcccca 180
 natggaagca gctgtgtatg caggagggg gcagaggctg ctgccaatgg gcatgtccct 240
 tacctgaaag ggccacctct ccaggtgaca tgtcctgggg gagccggggc cgtctgctcc 300
 ggccagaggc gctcagctca ggccacacca ggccaggcac ctcccaacct ggacagggtg 360
 ggaccaaggt ggccttgac aaaactctct gtgtttgcc aagcaccat cggacacaga 420
 gagtcaacca caccacagtc acatggtgtc cacacngcag ggggtcaagga ggcccgccc 480
 ctccccctca gacgtccctg ggcctctggg agtcagcaag gacgaggacg gcattgccct 540
 tcgagacagg aaggagtgga cctcctcccg gcggcatcca ggctcngctt ctccggagag 600
 gagagggggc tacttgctgg ataaancggc cggggccaca gagaaaaagc aaggtagacca 660
 tgagcacctt gcaaacacag tgcacccacc agcatttnag caccnnggac tgtgaagacc 720
 tccccattct tcggggggaa acncgccaa ngttccccc accntcacta gtgnattgtg 780
 acctgggggn cgggcccagc cctgtngctt gggnnagccc tccncccagg tttctnnggc 840
 ngcccnttaa nggncctng nttggccctt tggcncctt tncgcttttc cca 893

<210> 747
 <211> 738
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(738)
 <223> n=A,T,C or G

<400> 747
 gatatcccgg gaattcgcgg ccgcgtcnao gaagcacaga cctgngccct gctctcatgg 60
 ggcagactgc catttgtcat tnattactga aggaaaggga tcctcagttt gcttgtggac 120
 atttcaaatt tgaggtgaga gttggataag taagaataaa gctgctcttc aaagagatga 180
 atatagaaaa agaaacaaga tacagncttg gcagtaaggc tgggaggaag gggaaaagg 240
 aataaagaat gaaagagtga gaaatgtgag caggagctga acacagaaaa gttcagngac 300
 agaagcnaaa ggagggaaga agggaggagg gtccctttca cagaggctca cgaggatgct 360
 ttatgngtgc catgcagtc atgttcagga tgtctgcttc ttanctctct acttttctaa 420
 tanaaatttg gatacttact gatcctacat atgtaacagg gagagaagggt gaatttcaaa 480
 gcantaaatt gaaaaattgt tcacaatttc attttttaaa aaaaggagc taacagaaga 540
 agaggttaatt ggggtaatta taggatgnct cttgcgacac atgaatgnat ctggtatcat 600
 ctgagtgggg ggggagctgt cttcctgacc caaaaggatc ctttcggtan ccngnactta 660
 ngtcccaaaa cctcaccacc ttggagaaat natttccttt tgggggtntc attaaancct 720
 tttggncccc gcaaaagc 738

<210> 748
 <211> 647
 <212> DNA
 <213> Homo sapiens

<220>

274.

<221> misc_feature

<222> (1)...(647)

<223> n=A,T,C or G

<400> 748

```

ctntgtggcg gtggctgtct catttgggtg gacttttttg gtcgtaggaa cctggtatng 60
aggtcgagag taagacgggc tattagtagt cgcacgagag ttatttgtga aaacctggtt 120
agggcctctg tctccgctgc gctcgcctaa attggtatgg ctcgacttgg aaacacggtt 180
ctaacacgcg ttgttagcgc ccttgctagc atgtgaagga cactggccct accaagaaag 240
attcgagtcg ctccctccgg tatcgttcac ggaggcgata tttactcttc ttactacggt 300
tacttcgaga ttgtctgtga agtttaagac tactaaaaag agtattaagc ctatcgggaa 360
ttagctagat cgacacgcta aaaccaaggg caatcggcgg aaatatagag gcaccaataa 420
tagggcctac agaaggcccg agggttagac tcacgtttta taccggccac gggagaaata 480
aaaagataaa gtatacatcg ttttagcggtc ctccgaagcc ttcggtttta atgccaagga 540
gtcgaagca tcgtcggcga gtaataaact ccacgcgcc gagactatct acgacgccct 600
ccttaanatc cgtaaattac tcccggaaag agtatntag cggtct 647

```

<210> 749

<211> 642

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(642)

<223> n=A,T,C or G

<400> 749

```

ctntgtggcg gtgntgtct catttgggtg gacttttttg gtcgtaggaa cctggtatgc 60
aggtccgcg agcgtgggtc ctgcgtcgtg atgttggggg ttggtgtggt gccggttgtt 120
tttggttctg ttgagcgtag tgtgtttgaa ggttagcggt cgtgtcttgc ttgtggtttg 180
gtgttttagg cgggtgggga ggttgttgt tagctgttgt atgtcatatt gttggtgttg 240
ctgccctgtg ctgtttgtcc ttggttattg tggttgttac cccgcctgtg tggaagtgtt 300
gtggcagggc ggaatttaa gtgggagagt tgtgggacct gtggttgttg ttacgttgc 360
gcttttgtcg tggcggttg cggcgctct gataattaga attggatacg gagtgtataa 420
tacttctagt aaatggggac ctagtgttgc acttcccga atagggatct atgcgaagtc 480
cttaggatag tctttgataa gtttaacgcc caccacccta aaattataca cgattagacg 540
cataacgact cctccaggaa agataaagaa tctcacatat agaacgggac ccatacacg 600
tcggatagga aacaagagaa ctaattttng ttaaaaagac tt 642

```

<210> 750

<211> 639

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(639)

<223> n=A,T,C or G

<400> 750

```

tttgtggcg tggtgtctca tttgggtgga tttttgggtc gtaggtaacc tggtatngag 60
gtatagatgc cgattggtcc cgacgagcgt caccgataaat tcggtagttt cgcccttttt 120
agaaggcgct agtactcgga acttcacttc atctcggtag tttacttttg cgtatatagc 180
cttctccctc gaagactagc cgtcacattc gttccctagg aatcgtttct gccctaaga 240
atccgagagc gagatccga aactagagga accttagaag agtcgtattt ccacaaggac 300
cccacagtca ttccgggaaa atccctagga ccatacgggtt aggattcccc cggaaccggg 360
agcaaagctc atgatttccc acaccgcgag agcgccctata accctatccc atttcttcgg 420

```

275

```

gttatcgagg atattacgat caagcogaga gaaccgctag aaccgctttc ttcgctttct 480
cacggaacct ataagtagaa agagaaactc aggtcttaag gggcgcttc ggctaacgaa 540
acttctactt acgaagagag tatctagaca ttaagtcata aaaatccact acgcacctcg 600
tgtacgatat catcgggagc ggttcataga cgggtgccg 639

```

```

<210> 751
<211> 637
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(637)
<223> n=A,T,C or G

```

```

<400> 751
cttttgtggc ggnggtgtct catttgggtg gatttttggg tcgtaggnaa cctgggtatng 60
aggcagctct gagccccccc ccccccccc cccccnccc ccccccccta ggnggttggg 120
aanaacgggtg atacctaaat cgagtgngtt cattaanaag agttgattac nccctaaaat 180
aanaanaggg cttcgtcggg anaaatcggg aagganaagt cttnttggca tcataanaat 240
actggctcgg gtcctaanaat nttaaggng gtcnccgagg gtnttcatac cgataanaaa 300
cgttttccta tcggcaacgg gcttacctga gggnggactt ctncgngnc ggngattnan 360
acgaanacgt agaggattnc cgntacttnt tganatcacn cgtatcatac ttgtaagcat 420
aatnttctctg aaaagtgtta taanaatacg cncgcataatt cgctttttcg tcctagggat 480
gcttaaatgg cgatactgct atagcgggtg agcgttgggt ctcgagnaan aaagcgtgtc 540
ctaatacgctc taaggnttta agnccgttgg tttaaaaata nccttagaaa cctcgaggcg 600
gatactggtt tntttttaac gaaacaaagc accccnn 637

```

```

<210> 752
<211> 644
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(644)
<223> n=A,T,C or G

```

```

<400> 752
tntgtggcgg tgggtgctcat ttgggtggat ttttgggtcg taggaacctg gtatgaggtc 60
ttgcgagttg ttggtgtgtc ctgtcgttcg gtggttccct tttgagttga gtttgtcctt 120
tgaggttgtt agctgctgtt cgtttgtgtt cgtgtagtgc tttgggttga gagggttatg 180
gtggtgggta cgggtgtattg tcgcccggtg tcgcggggtt ggggtggtcg tcggttttgt 240
ggttcatagt agtcttctgc gttcggtggt gcgggttttg gtgagtagtt tcgttcttgg 300
atgtcccat gaccgcctat aatctaagta agggttagta gaaacctctc ccgatagac 360
acaaccgtcg tccactaaag acctcgctc tgatttttaa aaggacccga aaaacatccc 420
ttcaacggaa aaaacggaaa aaaagtcagc gaattcaaag aagccacggg agagaaaaaa 480
gaactaaagt tagtccgtca ttatatgtct cctcggagga ggaagcggcg gtggcggaaa 540
atgaggcggg aagaaagacg acctctatcg gcggcctang ccctaaaagg gcgatacctt 600
acgggatgat aaggacccta ggacgcctcc ttctcgatc gtcc 644

```

```

<210> 753
<211> 635
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

276

<222> (1)...(635)

<223> n=A,T,C or G

<400> 753

```

ctttgtggcg gtggtgctca tttgggtgga tttttgggtc gtaggaacct ggtatgaggg 60
aatcagctcg accccccccc cccccccct ccgaagcaga gcccaaccca aagtccaccg 120
actaccgag taaactctcg gagggtagaa taagaaggag taggtcctag ccaatagaag 180
tagttccgag cgttaggac agcggacgga acattnaaga aagagcctat attagggagg 240
aagtaacgtt cctctttcgg agctctttaa ggggtagtcc cagaacaagg gaagaggacc 300
cgtcggctat tgcccgtcga tacgggctct cacggngagc ctaggttcga ggatagggcc 360
gctcgtaaaa ttatacgggt tccgagaaac gcttccgtag accgggtcct aaatcgtccg 420
gagtattngg agagggatcc ttcggaccct agggacagag agaggagaac ggaggttaca 480
ggaggagaac gtntcctcnc tagttttctt tangtcgaaa aatttccttac cgataggggt 540
cctagggctg gngaatttac ggttcgaaaa acggtagtnc ctaanggntg ntattngggg 600
tagtatcggg tcgtttacaa ntcgtccgtc ttntg 635

```

<210> 754

<211> 721

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(721)

<223> n=A,T,C or G

<400> 754

```

accggattng ttncgtgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360
ccctaagac agaggagaa taaggagttc tccccatgat ggaaaatatc caaagacaag 420
gtttcatgga gcaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc tttgcttctt cccaccctc tttcccagct ctctctctgt 540
ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn ttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tccccctga 660
ataggggatt ctntangccc tgagaatttc nttatcanaa aaatatattt ttaaagcatt 720
a 721

```

<210> 755

<211> 721

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(721)

<223> n=A,T,C or G

<400> 755

```

accggattng ttncgtgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360

```

277

```

ccccataaagc agagggagaa taaggagttc tccccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgtcttctt cccaccctc tttcccagct ctctctctgt 540
ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn tttccccttt 600
ttaatcttct atantcttaa ncctaccaan ggccctcnt gannaatttn tcaccctga 660
ataggggatt cntangccc tgagaatttc nttatcanaa aaatatTTTT ttaaagcatt 720
a 721

```

<210> 756

<211> 873

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(873)

<223> n=A,T,C or G

<400> 756

```

ggaagaatac agtaagtttg caaattaaaa tttctctatt tttctgttat ttattcattt 60
ggaaactgtc agcctgtctc tttcactttg ggcaagtga agcaaagacg tccagtccta 120
tcagcaatta ggctgaaagt caacgccaag ctggcgggca agggctggtc tgagtagagg 180
ttccctaggc aggcaagaga gagactcca ctcgatactc ccagctcggc aactgcctga 240
atgccaatga gcactcatta taaccgccc tattttatag gatttaattt tacacttcag 300
gcttaatcag tctgaaagt aaactgacag tggttaagtt cggaatcaat gacatttagg 360
ctttatgact ttgtagctga atatctatgg gctatatttc cattctaaca gtgatatcct 420
gttccagaat ctcatctttt ggtgatggca ctttctagtg gagcagtcag ggtaacagtc 480
cacacccatt accatgtggg tgctttacag catactgacg gaaggactga ggagccaccg 540
gagcaggagt tctctcaggg gaggacgtg acacttcac agctgcctan gtatgggcac 600
ctgatgccaa cgaanaaccc aaagcgctct cccttcaga tggagctgc cccacactgg 660
gctgacagca tctggagctg ctctggctca aatcccgaa tcgcacanct octancgggg 720
gcgtttanag atcctcnggg ccagctaccg accacttttg acaagggmct taggagcgat 780
aactagnctg gcgcgttaca cncggatgga acgtcttgga cttgagacct cttgggggan 840
atggcncccc caaataantt gggaaaaantn ggg 873

```

<210> 757

<211> 782

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(782)

<223> n=A,T,C or G

<400> 757

```

ggccccctga gggatactct agagcgggcg ccgactagt agctcgtcga cgatatcccc 60
ggatttgaga ccaggagaca gctccagatg ctgtcagccc agtgctgggg gcaggcttcc 120
atctgtgaag tggagaggcg ctttgggctt ctctgtggc atcaggtgcc catacctagg 180
gcagctgtgg aagtgtcagc gtctccctg agaggaaact ctgctccggg ggctcctcag 240
tccttccgtc agtatgtgt aaagcaccca catggtaat ggtgnggact ggtaccatga 300
ctgntccctt aaaagtggtg cttcccaag aaaggagaat tcttggaana gggatttcac 360
ttgnttagaa atgggaaaaa ttaccatta gaattttcgn ttccaaggcn tnaagnccta 420
aaaggccttt gattccccga ccttaaccct gggcagttta cctttcaaac gggataaacc 480
ctgangugga aatnaaatc ctttaaaaaa gggggggttt naaggagggc tctttggctt 540
tcaggcantt gccaacctgg gaaattcana ggggaagtnt tttttttgc ctgcctagg 600
aacctttact taaacnaacc cttgncccc ctttgggggt tgactttcan cctaattgct 660
gaaaggaccg ggccgntttt gntttccttt gncccaaagg naaanaaacg ggtgccantt 720

```

278

cccangggat tanttcccgaa aaatttggnn aatttttntt tgnaactttt tgggtttttt 780
cc 782

<210> 758
<211> 647
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(647)
<223> n=A,T,C or G

<400> 758
ntttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60
gggaagagcg ccgtcgggtcc gagtacagta tggagtagta tagtcttcgc gccttctcgg 120
gcggcggggc tattctctcc aaaggcagag gtccctagtc gacctcgctc ccctagggtta 180
ggaacagccg tcgaatattt taggttcgtc gaggctttct tccgagctct acgcctaagt 240
agctccgcga gcaaaagtac ggtcattttc ccctatccat cactccccta agtacgcctc 300
attattccgg aaggcaagag gccagcattc ctccttagag tagagggtag gtacctccgt 360
cgcggtgcgc gaaagggcag agcttcgtgt cttccctccg cagcagctta acggtctacg 420
taggcgttct cgatcttttc acgggaatcg gggtcgggga gggcggcgga aaacgtcgac 480
gtctcgggtca ccgtcaccgc ccgaacaac tagcggcttt ccgctttcaa ctgaggaacc 540
ccgcacccct cattagcgct tacgaaatcg gggangtgat tgcgccaatt cgtagcctt 600
cgataaattat tctctattag cggtcctatc tcgcgcttcc gatttat 647

<210> 759
<211> 657
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(657)
<223> n=A,T,C or G

<400> 759
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60
gggctctata gaaagcctct tgtctttaga tacgggcttt ctggtccttc gttctggaag 120
tgtagtagta ggtactgcgg gaaggcgaag agtcctttca aggacgattt acttaagttg 180
gcttattcta tagttccttc gggacataag gtcggtacga tctatactgc gtgggaagct 240
gataggttgg gacttaaggc gaataagaag gaggcggcgg aggtcgcgat taccgcagag 300
atattattta cggcggccgc gggtagccgc ggtcatgcgg aaattttctg aggttcttgg 360
attcctaaga tcgctcccggt cgagtatact agcgacgaac gtaagagtgc cctcacaaga 420
accggtacaa actcaagaag aagttcccat taagcatcgt aagaaacggg aggacgagga 480
cggtaagaag taatcggaga aaggatccta gtngttacga agaagcatcg ttnagctact 540
ttgcgctacc gtttatattt agacgtgttc cgtccttctc cgtgtttana aaaaagggtt 600
attccgacgg gagacttagg cgaatggagg gttccgcggg tganaatcgg ancgggg 657

<210> 760
<211> 644
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(644)
<223> n=A,T,C or G

279

```

<400> 760
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatgna 60
ggaaaagaag taagcctcga agcctatctc cgaccgtatt tatttcgcag aagacggaac 120
tacggacgtc gttaaccccg agtagccccc gtaagaaagg actaaagcga atggaaaagt 180
cggaattcc ggcgaggagg cggcgattac tgaaaggagt aagagtaaga ctattgcgat 240
acttgaggcg ttccctctta aaaggcacc cgaacactct attaaaaaac acccgaagaa 300
gaacaactca tgcgatcggc cgtgtgcagc cgtcaatagt aaagagagcc atgaaccatg 360
ccatccttag accaattagg atgaagaaga ggaggaagat gaggaccaa ccctaccac 420
tcgaaaaacc ccgcacgagc ctccgaacaa aatccgggaa ttaaacggc ggccacttc 480
cgcactctcg tagcgcggac cgaatagaaa accggaaact acagctaaag ggtcctttcc 540
ggcctgttat ctaccaccc gcaatccgat cctccccc cctcgtccaa aaaccctaac 600
ctctgcggca acattagagc agaaggagag ggcgatccct tgan 644

```

```

<210> 761
<211> 647
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(647)
<223> n=A,T,C or G

```

```

<400> 761
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60
ggcgggtact ctctgggata atcggtataa gtgtttgtaa attgggggta agagaaagt 120
tcattataag aagtggaagc acgagccggg gtgttttagt gttaatatta agaccggtt 180
ttgtttgact tatatagctt gcgcgtgggg aggcaataag aaacattgcg ttctgaggcc 240
ggatgcgggg aaccctcttc ggggtctaga gcgcgcgcat tgcaaaataa ggactactga 300
cgccgctcat aacgtactca acaatgagtc ggcctgcatt aagatttcgg cgaagaaccg 360
tactgcgtct actgatagta tattgcattg atagcggcat gagctttatc acgtgtcgtt 420
ttcgggttgt aagaaggag ttaagtcgat cttcgaggaa gaagagacc caaataaaaa 480
atgactcaaa aaaacctaga agaaacacga cgaaaggaaa aagaacgtta aaactagtag 540
ctcttcggan gagtagcctt agtagggtaa gtcctccgtg cgtactgtcc taaggtttgg 600
atagcgcggt tgaatagacg gtcacgcgtc agaaggtaaa aancgg 647

```

```

<210> 762
<211> 628
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(628)
<223> n=A,T,C or G

```

```

<400> 762
cattgtgttg gggctactga gccactttt ttccagattt tttgtaaaat tgtttcgcat 60
tgtgttccct ttattcgctt gtattaatat ttgcgtagt gattaaacaa atacttggtg 120
ttgactgtca gtcttagagg actgactaga agtagttttc atttggggct caggaaatac 180
ctactttata tttctagcta attaggaaag tcatttttca gttagggttg tgttttggtt 240
caggcactcg ctagctagat gacctaacat gctacttaat ttctgagtgt ttgtgtccat 300
ccctgtagga ttgttcggg gttaaatgaa atttgttata tttgtaaagc atttacctca 360
gtgccagac tgtgacagag tagattatta ggcttgctct tatttctgtg attaaattta 420
gtgtcagatt agaacctat agctacttct aaagctgctg ctgctttctt tgtttagggt 480
taggaagaaa catgctggac agtttgccaa atgagagtta catgatgtgg cttgtgggaa 540
cattctaact tggaacttgc ccatttccag gactttgnng ttcanagatt tttggggata 600

```

280

gatgtaaggg ttataaaaaa cngaaaac

628

<210> 763

<211> 147

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(147)

<223> n=A,T,C or G

<400> 763

cattgtgttg gggcagagat aaataattcc tctgaaaagt gttttattgg aatttcaaatt 60
gaaaagctaa ctggataact tacagcatgt ttctgccaat aatctcttan aacaggcctc 120
ttttttttat gcacaccacc ttcnngc 147

<210> 764

<211> 146

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(146)

<223> n=A,T,C or G

<400> 764

cattgtgttg ggtatgtttt ttgaaggcag gtggacagga tttgctgatg ggtaaatggc 60
agagttaggg ggactgttag aacagagaaa.ganatcatgg ggttgggtt gagtctgatg 120
nnnaactggg gccgnntgct cagtat 146

<210> 765

<211> 129

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(129)

<223> n=A,T,C or G

<400> 765

tncncgattc gntnctagcg tntacactna tgtcttggtta ccgagctcgg atccactagt 60
ccagtgtggg nggaattcca ttgtgttggg gcaggaggng ctttgngtac ngtgcggctg 120
nagaggcgg 129

<210> 766

<211> 175

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(175)

<223> n=A,T,C or G

<400> 766

281

```
cattgtgttg ggcctagtc gaatactttt agtaacttca gacagatctc ctcatctctt 60
tctggggctt ggnnttttctc ctttgtanaa tgatgccttt ctgtgggttt gtcattttcta 120
acattctgtg ngtgatgagg tgtatattcg anganctcta tcncanagt actct 175
```

<210> 767

<211> 602

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(602)

<223> n=A,T,C or G

<400> 767

```
nnntttaaaa nctgtntctcc ccgcgggtggc ggccgctcta gaactagtgg atcctttcca 60
cctggtttgt tttcagtgtt taatcctatt agtatcagca ggatataggc caggatatca 120
ggtgcagaac ctgtggaatc agccaatttg gcttgctcat ttactttaat aagggtcccat 180
aatgagttag agtacaaaag tcaagccctg ttgaggggtc gcattaaact ctcagaagta 240
tttagagtgt gccaggagcc gcgaaggctc ggttcgggtg gtggcgggaa ctgtattaga 300
gtgctaggca cggcgcgaca aagtctgtcc aacccaaaac ggtgctgagg cgttgggtgt 360
gagctccagt actcagaaaa gcctctcagc aggtactcaa cagatcctca ggggcttggg 420
ggcccagcac tggcagttag ggcatgaaag acataaaagg gcactacctg tgggtatttt 480
ctgttctcca aggaggaagt agcaaaaatt aggacgctgg aatatcctat gttgtagcaa 540
tcccagaaca actgatgctc aacaaatacc acacaaaaca aattttttaa aatttaactc 600
ta 602
```

<210> 768

<211> 671

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(671)

<223> n=A,T,C or G

<400> 768

```
tccaccgcgg tggcggccgc tctagactag tggatccact agtccagtgt ggggtgggaat 60
tcgcggcncg cgtcgacaaa aatactgcta aagtaatat tttatagatg actatttgcc 120
ttggggccag gaaaagcagc tggagttatt cacttagtac catttttaca tactaacttt 180
gccttttcca tgcttgcttg atgcggcttg cagcactgaa gaacagtttc aattgctagc 240
caaccagaga gcatgatcaa accaaacaag ttccctgttt caggaaaaac aggttttagg 300
taactgaagg gttaccagt actgattcca caatcttctc tgtaaaanatttctgcctat 360
tatgcagact gggcggcctt aaanntggta aaactatnaa ataccctac aatattttta 420
nggggccccn ttatnaagct tttcaggcct tcccctttcc atagcattgg tgggatacaa 480
gaaaccttta aacagcaacn agctatcnag gcccaaaagg aaagtaattn tgatttttta 540
nagattccgn aacgaaaaaa tggctgggtt caaatacnac cttcttttta aaatggnntc 600
cttattaaac nttttttttt ttttaattta ccccatgggtc ntgatnttng ngcttccgcc 660
canaaaatng n 671
```

<210> 769

<211> 877

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(877)

<223> n=A,T,C or G

<400> 769

```

aaagctggag ctccccgcgg tggcggccgc tctagaacta gtggatccac tagtccanng 60
ngggggaatt cgcgggccgc tgcacctcta tacctttgnt catgcagctt cctctgactg 120
ggtttggtct tcaattggct aacccctctt ttacttaagc acaccttgaa cattccctcc 180
ttccccattt cccgcgagng cccctaattg acatacttct gaataacaca ggtggtattc 240
cttccttggt ggaacctcct ggaggaagag acagatgatt aacaaatcct tccatcaacc 300
cctttgacca tgacatcaac agtgctccaa attatgggtt accgtattag cctatgtcta 360
tcttgatcag aatccttacc tcggtgtatt gaaattatct atttcgtgcc tgcctcttta 420
aagtcagggt ttgccttacc tattgtctaa caccatgcag taggtaacat gcagtaggaa 480
acatggcatt aaattatttg ggttcaaadc ccagttatgg tgtgtaaatg cctaccaggc 540
cgtgaggcac ctgctaagca ggttgcaagc atcatttgaa ttcacaccac ccttttgcaa 600
tagaacagat aggcaacaga ggctcatttg ggctaaagga tttgatggag gggaaagtgc 660
aggattccca ccaaggcctc anggccaggg tccanggacc atgtctgttg tgacaactgg 720
agtgcatttc atatcccctn ctctgngggg naaggtccct cncgnggaga acnnttaaaa 780
caatcatntc tngggggntt aatgcttctt nccccagtg gttncaactgc ngccacgagt 840
cccancact agtcccangt ctgtcatgaa ccancccc 877

```

<210> 770

<211> 874

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(874)

<223> n=A,T,C or G

<400> 770

```

ctggnetccc cgcggtggcg gccgctctag aactagtga tccactagtc cagtgtggtg 60
gaattcgcg cgcgctcgac cttttcaaag gtttaacttat ttaattatca canngcaac 120
ccgatgagta ggtaacagta ttttactgat aggtaatcta aagaaggagg ctaaataaat 180
tgcccaattt cgaacagtga gaggaagaat taggattgaa acacatatag tggcttcaga 240
atctgtaacc ctacgatgc cactactact tctttcagaa taccctttgc ctatctattc 300
tgttcctatg tcatcaaatt ataacttact taaaaagtat ttgtctttat tattttttaa 360
aaaacacagg gaagtatttc tgatcagggg cagtattggt tctgaaagac aagccagtg 420
ttttgagggt ttctcccttg ccagtttttc tatgctgggt tattcaagtc ctaagaattg 480
tgtagctatt acagaaccgc tttagcaaat gtgttcatt aatcaagggt atttataaca 540
aaatttcac caagtttgga gtgctctgaa aacatagcca aaatgttcgc agggctctac 600
cctctcggt gtccctttt tttagctatt tcagaagcac actggtgcaa tattttacga 660
aatgagtttc ttccctttac ctctgcaccc tctaagaaaa aatcattgnt gttttatgaa 720
natgaanatc ctgctatttc atatcttgat tggagctgct taattaaatg accattttta 780
aatttgtttt gattccnngc aaaaaaagtt tnttnttgga tgtagggggc tcnnaaagnc 840
caaaaccccc caaaattttt nnttggaac ccona 874

```

<210> 771

<211> 156

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(156)

<223> n=A,T,C or G

<400> 771

283

```

ttaaaaaanct ggncctccccg cggtggcgccg cgctctagaa ctagtggatc cactagtcca 60
gtgtgggtgga attcgcgccg gcgtcgaccg cgagcggtcg cccttttttt tttttttttt 120
ngtttttttg aanaattcat tgggtattta ttattc 156

```

<210> 772

<211> 586

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(586)

<223> n=A,T,C or G

<400> 772

```

ncaanctggg ctccaccgcg gtggcgcccg ctctagacta gtggatccac tagtccagtg 60
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tccagatatg aaacttaccc ccagctatgg tcttctatct gttatttaat ttctaggcca 180
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<212> DNA

<213> Homo sapiens

<400> 773

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<213> Homo sapiens

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Arg Thr Pro Ser Asp His Tyr Asn Trp Gln Ala Thr Leu Gln Asn Glu
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Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile
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Leu Gly Lys Tyr Gln Leu Asn Val Lys Thr Gly Asn His Ile Leu Lys
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Lys Pro Trp Asn Phe Gly Gln Phe Glu Lys Asn Val Leu Asp Cys Cys
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<212> PRT

<213> Homo sapiens

<400> 778

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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
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Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
                85              90              95
Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
                100             105             110
Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
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Tyr Gly Leu Thr Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
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Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu	260	265	270
Glu Lys His Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly	275	280	285
Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu	290	295	300
Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val	305	310	315
Glu Gly Ser Gly Arg Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val	325	330	335
Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe	340	345	350
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Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val	370	375	380
Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser	385	390	395
Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn	405	410	415
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<212> DNA

<213> Homo sapiens

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Val	Arg	Leu	Phe	Leu	Glu	Asn	Gly	Leu	Asn	Leu	Arg	Lys	Phe	Leu	Thr
465					470					475					480
His	Asp	Val	Leu	Thr	Glu	Leu	Phe	Ser	Asn	His	Phe	Ser	Thr	Leu	Val
				485					490					495	
Tyr	Arg	Asn	Leu	Gln	Ile	Ala	Lys	Asn	Ser	Tyr	Asn	Asp	Ala	Leu	Leu
		500						505					510		
Thr	Phe	Val	Trp	Lys	Leu	Val	Ala	Asn	Phe	Arg	Arg	Gly	Phe	Arg	Lys
		515					520					525			
Glu	Asp	Arg	Asn	Gly	Arg	Asp	Glu	Met	Asp	Ile	Glu	Leu	His	Asp	Val
	530					535					540				
Ser	Pro	Ile	Thr	Arg	His	Pro	Leu	Gln	Ala	Leu	Phe	Ile	Trp	Ala	Ile
545					550					555					560
Leu	Gln	Asn	Lys	Lys	Glu	Leu	Ser	Lys	Val	Ile	Trp	Glu	Gln	Thr	Arg
				565					570					575	
Gly	Cys	Thr	Leu	Ala	Ala	Leu	Gly	Ala	Ser	Lys	Leu	Leu	Lys	Thr	Leu
			580					585					590		
Ala	Lys	Val	Lys	Asn	Asp	Ile	Asn	Ala	Ala	Gly	Glu	Ser	Glu	Glu	Leu
		595					600					605			
Ala	Asn	Glu	Tyr	Glu	Thr	Arg	Ala	Val	Glu	Leu	Phe	Thr	Glu	Cys	Tyr
	610					615					620				
Ser	Ser	Asp	Glu	Asp	Leu	Ala	Glu	Gln	Leu	Leu	Val	Tyr	Ser	Cys	Glu
625					630					635					640
Ala	Trp	Gly	Gly	Ser	Asn	Cys	Leu	Glu	Leu	Ala	Val	Glu	Ala	Thr	Asp
				645					650					655	
Gln	His	Phe	Ile	Ala	Gln	Pro	Gly	Val	Gln	Asn	Phe	Leu	Ser	Lys	Gln
			660					665					670		
Trp	Tyr	Gly	Glu	Ile	Ser	Arg	Asp	Thr	Lys	Asn	Trp	Lys	Ile	Ile	Leu
		675					680					685			
Cys	Leu	Phe	Ile	Ile	Pro	Leu	Val	Gly	Cys	Gly	Phe	Val	Ser	Phe	Arg
	690					695					700				
Lys	Lys	Pro	Val	Asp	Lys	His	Lys	Lys	Leu	Leu	Trp	Tyr	Tyr	Val	Ala
705					710					715					720
Phe	Phe	Thr	Ser	Pro	Phe	Val	Val	Phe	Ser	Trp	Asn	Val	Val	Phe	Tyr
				725					730					735	
Ile	Ala	Phe	Leu	Leu	Phe	Ala	Tyr	Val	Leu	Leu	Met	Asp	Phe	His	
			740					745				750			
Ser	Val	Pro	His	Pro	Pro	Glu	Leu	Val	Leu	Tyr	Ser	Leu	Val	Phe	Val
		755					760					765			
Leu	Phe	Cys	Asp	Glu	Val	Arg	Gln	Trp	Tyr	Val	Asn	Gly	Val	Asn	Tyr

296

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      770      775      780
Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785      790      795      800
Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
      805      810      815
Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
      820      825      830
Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
      835      840      845
Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
      850      855      860
Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865      870      875      880
Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
      885      890      895
Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
      900      905      910
Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
      915      920      925
Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
      930      935      940
Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
      945      950      955      960
Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
      965      970      975
Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
      980      985      990
Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
      995      1000      1005
Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
      1010      1015      1020
Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
      1025      1030      1035      1040
Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
      1045      1050      1055
Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
      1060      1065      1070
Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
      1075      1080      1085
Glu Ile Ala Asn Lys Ile Lys
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298

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<210> 797

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<211> 45
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5 10 15

<210> 801
<211> 15
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5 10 15

<210> 802
<211> 15
<212> PRT
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<400> 802
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300

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<210> 804

<211> 15

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<211> 15

<212> PRT

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<210> 806

<211> 15

<212> PRT

<213> Homo sapiens

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Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
5 10 15

<210> 807

<211> 15

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<211> 15

<212> PRT

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<210> 809

301

<211> 17
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Ser

<210> 810
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<210> 811
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<210> 812
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<210> 813
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<210> 814
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302

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 5 10 15

<210> 815
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<220>
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 aagaaacgag aatgtgtctt ctttaccaaa gattccaagg ccacggagaa tgtgtgcaag 180
 tgtggctatg ccagagcca gcacatggaa ggcaccaga tcaaccaaag tgagaaatgg 240
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303

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<211> 652

<212> PRT

<213> Homo sapiens

<400> 818

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			20					25					30		
Val	Asn	Phe	Ile	Gln	Ala	Asn	Phe	Lys	Lys	Arg	Glu	Cys	Val	Phe	Phe
		35					40					45			
Thr	Lys	Asp	Ser	Lys	Ala	Thr	Glu	Asn	Val	Cys	Lys	Cys	Gly	Tyr	Ala
	50					55					60				
Gln	Ser	Gln	His	Met	Glu	Gly	Thr	Gln	Ile	Asn	Gln	Ser	Glu	Lys	Trp
	65				70					75					80
Asn	Tyr	Lys	Lys	His	Thr	Lys	Glu	Phe	Pro	Thr	Asp	Ala	Phe	Gly	Asp
				85					90					95	
Ile	Gln	Phe	Glu	Thr	Leu	Gly	Lys	Lys	Gly	Lys	Tyr	Ile	Arg	Leu	Ser
			100					105					110		
Cys	Asp	Thr	Asp	Ala	Glu	Ile	Leu	Tyr	Glu	Leu	Leu	Thr	Gln	His	Trp
		115					120					125			
His	Leu	Lys	Thr	Pro	Asn	Leu	Val	Ile	Ser	Val	Thr	Gly	Gly	Ala	Lys
	130					135					140				
Asn	Phe	Ala	Leu	Lys	Pro	Arg	Met	Arg	Lys	Ile	Phe	Ser	Arg	Leu	Ile
	145				150					155					160
Tyr	Ile	Ala	Gln	Ser	Lys	Gly	Ala	Trp	Ile	Leu	Thr	Gly	Gly	Thr	His
			165					170						175	
Tyr	Gly	Leu	Met	Lys	Tyr	Ile	Gly	Glu	Val	Val	Arg	Asp	Asn	Thr	Ile
		180						185					190		
Ser	Arg	Ser	Ser	Glu	Glu	Asn	Ile	Val	Ala	Ile	Gly	Ile	Ala	Ala	Trp
		195					200					205			
Gly	Met	Val	Ser	Asn	Arg	Asp	Thr	Leu	Ile	Arg	Asn	Cys	Asp	Ala	Glu
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Gly	Tyr	Phe	Leu	Ala	Gln	Tyr	Leu	Met	Asp	Asp	Phe	Thr	Arg	Asp	Pro
	225				230					235					240
Leu	Tyr	Ile	Leu	Asp	Asn	Asn	His	Thr	His	Leu	Leu	Leu	Val	Asp	Asn
			245						250					255	
Gly	Cys	His	Gly	His	Pro	Thr	Val	Glu	Ala	Lys	Leu	Arg	Asn	Gln	Leu
		260						265					270		
Glu	Lys	Tyr	Ile	Ser	Glu	Arg	Thr	Ile	Gln	Asp	Ser	Asn	Tyr	Gly	Gly
	275						280					285			
Lys	Ile	Pro	Ile	Val	Cys	Phe	Ala	Gln	Gly	Gly	Gly	Lys	Glu	Thr	Leu
	290					295					300				
Lys	Ala	Ile	Asn	Thr	Ser	Ile	Lys	Asn	Lys	Ile	Pro	Cys	Val	Val	Val
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Glu	Gly	Ser	Gly	Gln	Ile	Ala	Asp	Val	Ile	Ala	Ser	Leu	Val	Glu	Val
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Glu	Asp	Ala	Leu	Thr	Ser	Ser	Ala	Val	Lys	Glu	Lys	Leu	Val	Arg	Phe

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      370      375      380
Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385      390      395      400
Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
      405      410      415
Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
      420      425      430
Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
      435      440      445
Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
      450      455      460
Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465      470      475      480
His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
      485      490      495
Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
      500      505      510
Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
      515      520      525
Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
      530      535      540
Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545      550      555      560
Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
      565      570      575
Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
      580      585      590
Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
      595      600      605
Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
      610      615      620
Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625      630      635      640
Ala Trp Gly Gly Leu Glu His His His His His His
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<210> 819

<211> 132

<212> PRT

<213> Homo sapien

<400> 819

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      20      25      30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
      35      40      45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
      50      55      60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
65      70      75      80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala

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305

			85					90				95			
Asp	Ala	Leu	Asn	Gly	His	His	Pro	Gly	Asp	Val	Ile	Ser	Val	Asn	Trp
			100					105					110		
Gln	Thr	Lys	Ser	Gly	Gly	Thr	Arg	Thr	Gly	Asn	Val	Thr	Leu	Ala	Glu
			115				120					125			
Gly	Pro	Pro	Ala												
			130												

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 <211> 36
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 <213> Artificial Sequence

<220>
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<210> 821
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<220>
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<400> 821
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<210> 822
 <211> 675
 <212> DNA
 <213> Homo sapiens

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 accgttcata tggggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180
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 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catgatccgg 420
 gagaaatttg ccactgcac cgtgctaacc attgcacaca gattgaacac cattattgac 480
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<210> 823
 <211> 291
 <212> DNA
 <213> Homo sapiens

306

<400> 823

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accattattg acagcgacaa gataatgggt ttagattcag gaagactgaa agaataatgat 120
gagccgtatg ttttgctgca aaataaagag agcctattttt acaagatggg gcaacaactg 180
ggcaaggcag aagccgctgc cctcaactgaa acagcaaaac agagatgggg tttcaccatg 240
ttggccaggc tgggtctcaa ctccctcgag caccaccacc accaccactg a 291

```

<210> 824

<211> 1074

<212> DNA

<213> Homo sapiens

<400> 824

```

atgtcagcca ttgagagggt gtcagaggca atcgtcagca tccgaagaat ccagaccttt 60
ttgctacttg atgagatata acagcgcaac cgtcagctgc cgtcagatgg taaaaagatg 120
gtgcatgtgc aggattttac tgcttttttg gataaggcat cagagacccc aactctacaa 180
ggccttttct ttactgtcag acctggcgaa ttgttagctg tggtcggccc cgtgggagca 240
gggaagtcac cactgttaag tgccgtgctc ggggaattgg cccaagtca cgggctggtc 300
agcgtgcatg gaagaattgc ctatgtgtct cagcagccct ggggtgttctc gggaactctg 360
aggagtaata ttttattttg gaagaaatac gaaaaggaaac gatatgaaaa agtcataaag 420
gcttgtgctc tgaaaaagga tttacagctg ttggaggatg gtgatctgac tgtgatagga 480
gatcggggaa ccacgctgag tggagggcag aaagcacggg taaaccttgc aagagcagtg 540
tatcaagatg ctgacatcta tctcctggac gatcctctca gtgcagtaga tgcggaagtt 600
agcagacact tgttcgaact gtgtatttgc caaattttgc atgagaagat cacaatttta 660
gtgactcatc agttgcagta cctcaaagct gcaagtcaga ttctgatatt gaaagatggg 720
aaaatggtgc agaaggggac ttacactgag ttccataaaat ctggatataga ttttggctcc 780
cttttaaaga aggataatga ggaaagtga caacctccag ttccaggaac tcccacacta 840
aggaatcgta ccttctcaga gtcttcggtt tgggtctcaac aatcttctag accctccttg 900
aaagatgggt ctctggagag ccaagataca gagaatgtcc cagttacact atcagaggag 960
aaccgttctg aaggaaaagt tggttttcag gcctataaga attacttcag agctgggtgct 1020
cactggattg tcttcatttt ccttattctc gagcaccacc accaccacca ctga 1074

```

<210> 825

<211> 224

<212> PRT

<213> Homo sapiens

<400> 825

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
                    5                10                15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
                20                25                30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
                35                40                45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
                50                55                60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
                65                70                75                80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
                85                90                95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
                100                105                110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
                115                120                125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala
                130                135                140
His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp

```

307

```

145          150          155          160
Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp
          165          170          175
Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met
          180          185          190
Val Gln Gln Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala
          195          200          205
Lys Gln Arg Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
          210          215          220

```

<210> 826

<211> 357

<212> PRT

<213> Homo sapiens

<400> 826

```

Met Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg Arg
          5          10          15
Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg Gln
          20          25          30
Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala
          35          40          45
Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe
          50          55          60
Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly Ala
          65          70          75          80
Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro Ser
          85          90          95
His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln Gln
          100          105          110
Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly Lys
          115          120          125
Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala Leu
          130          135          140
Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile Gly
145          150          155          160
Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn Leu
          165          170          175
Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp Pro
          180          185          190
Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu Cys
          195          200          205
Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His Gln
          210          215          220
Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp Gly
225          230          235          240
Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly Ile
          245          250          255
Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln Pro
          260          265          270
Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu Ser
          275          280          285
Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly Ala
          290          295          300
Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu Glu
305          310          315          320
Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr Phe

```

308

325 330 335
 Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Glu His
 340 345 350
 His His His His His
 355

<210> 827
 <211> 96
 <212> PRT
 <213> Homo sapiens

<400> 827
 Met Gly Ile Arg Glu Lys Phe Ala His Cys Thr Val Leu Thr Ile Ala
 5 10 15
 His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys Ile Met Val Leu Asp
 20 25 30
 Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr Val Leu Leu Gln Asn
 35 40 45
 Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln Leu Gly Lys Ala Glu
 50 55 60
 Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg Trp Gly Phe Thr Met
 65 70 75 80
 Leu Ala Arg Leu Val Ser Asn Ser Leu Glu His His His His His His
 85 90 95

<210> 828
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 828
 cgcccatggg gatccgggag aaatttgccc actgc 35

<210> 829
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 829
 cgcctcgagg gagtttgaga ccagcctggc caaca 35

<210> 830
 <211> 38
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 830

309

gcatggacca tatgtcagcc attgagaggg tgtcagag 38

<210> 831
 <211> 34
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 831
 ccgctcgaga ataaggaaaa tgaagacaat ccag 34

<210> 832
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 832
 gttgaattca tgcacgggcc ccaggtg 27

<210> 833
 <211> 30
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 833
 cccctcgagt cactatgggtc tgcctcttga 30

<210> 834
 <211> 915
 <212> DNA
 <213> Homo sapiens

<400> 834
 atgcatcacc atcaccatca cacggccgag tccgataact tccagctgtc ccaggggtggg 60
 cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
 accgttcata tcgggcctac cgccttctc ggcttggtg ttgtcgacaa caacggcaac 180
 ggcgacagag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
 ggcgacgtga tcaccgcgt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300
 gcgcttaacg ggcacatcc cggtgacgtc atctcggtga cctggcaaac caagtcgggc 360
 ggacgcgtga cagggaacgt gacattggcc gagggacccc cggccgaatt catgcacggg 420
 cccaggtgc tggcacgctg ctccgagtg gcttgcctg ccttggtgc cacctctgcg 480
 ggggtgcgtc tggaggggtt ggaccggcca ccaaccttac ccagtcaagg aagtggatgg 540
 ccatgttccc acagcctgag tggctgccac ctgatggctg atggagcaaa ggccttagga 600
 aaagcagatg gcccttggcc ctaccttttt gttagaagaa ctgatgttcc atgtcctgca 660
 gcgagtgagg ttggtggctg tgccccagc tcctggcgcg ccctcgaga ggtgactggg 720
 tgctcttttg gccctcttgg ccttgcccag catgcacaag cctcagtgt actactgtgc 780

310

tacaaatgga gccatatagg ggaaacgagc agccatctca ggagcaaggt gtatgctgcc 840
 ttggggggct ccagtccttg cctcaagggt cttatgtcac tgtgggcttc ttgggtgtca 900
 agaggcagac catag 915

<210> 835
 <211> 304
 <212> PRT
 <213> Homo sapiens

<400> 835
 Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
 5 10 15
 Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
 20 25 30
 Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
 35 40 45
 Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
 50 55 60
 Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
 65 70 75 80
 Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
 85 90 95
 Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
 100 105 110
 Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
 115 120 125
 Leu Ala Glu Gly Pro Pro Ala Glu Phe Met His Gly Pro Gln Val Leu
 130 135 140
 Ala Arg Cys Ser Glu Cys Ala Cys Pro Ala Leu Ala Ala Thr Ser Ala
 145 150 155 160
 Gly Val Arg Leu Glu Gly Val Asp Arg Pro Pro Thr Leu Pro Ser Gln
 165 170 175
 Gly Ser Gly Trp Pro Cys Ser His Ser Leu Ser Gly Cys His Leu Met
 180 185 190
 Ala Asp Gly Ala Lys Ala Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr
 195 200 205
 Leu Phe Val Arg Arg Thr Asp Val Pro Cys Pro Ala Ala Ser Glu Val
 210 215 220
 Gly Gly Cys Ala Pro Ser Ser Trp Arg Ala Leu Ala Glu Val Thr Gly
 225 230 235 240
 Cys Ser Leu Gly Pro Leu Gly Leu Ala Gln His Ala Gln Ala Ser Val
 245 250 255
 Leu Leu Leu Cys Tyr Lys Trp Ser His Ile Gly Glu Thr Ser Ser His
 260 265 270
 Leu Arg Ser Lys Val Tyr Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu
 275 280 285
 Lys Gly Leu Met Ser Leu Trp Ala Ser Trp Leu Ser Arg Gly Arg Pro
 290 295 300

<210> 836
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 836

311

cgaagtcacg tggaggccag cctc

24

<210> 837

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 837

cctgaccgaa ttcattaact ggcctggac

29

<210> 838

<211> 166

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> (1)...(166)

<223> Xaa = Any Amino Acid

<400> 838

Met	Gly	His	His	His	His	His	His	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg
1				5					10					15	
His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile
		20					25					30			
Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser
		35					40					45			
Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly
	50					55					60				
Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val
65					70					75					80
Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro
				85					90					95	
Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Xaa	Gln	Xaa
			100					105					110		
Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr
		115					120					125			
Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly
	130					135					140				
Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu
145					150					155					160
Lys	Thr	Val	Gln	Ala	Ser										
					165										

<210> 839

<211> 504

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(504)

<223> n = A,T,C or G

312

<400> 839
 atggggccatc atcatcatca tcacgtggag gccagcctct ccgtacggca cccagagtac 60
 aacagaccct tgctcgctaa cgacctcatg ctcatcaagt tggacgaatc cgtgtccgag 120
 tctgacacca tccggagcat cagcattgct tcgcagtgcc ctaccgcggg gaactcttgc 180
 ctcgtttctg gctgggtct gctggcgaac ggcagaatgc ctaccgtgct gcagtgcgtg 240
 aacgtgtcgg tgggtgtctga ggaggtctgc agtaagctct atgaccgcgt gtaccacccc 300
 agcatgttct ggcgcggcgg agggcaanac cagaangact cctgcaacgg tgactctggg 360
 gggcccctga tctgcaacgg gtacttgag ggccttgtgt ctttcggaaa agccccgtgt 420
 ggccaagtgt gcgtgccagg tgtctacacc aacctctgca aattcactga gtggatagag 480
 aaaaccgtcc aggccagtta atga 504

<210> 840
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 840
 ctcagggttc cggagccgcg g 21

<210> 841
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 841
 ctatagaatt cattaccaa aagctgggct ccagc 35

<210> 842
 <211> 241
 <212> PRT
 <213> Homo sapiens

<400> 842
 Met Gln His His His His His His Leu Arg Val Pro Glu Pro Arg Pro
 1 5 10 15
 Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro
 20 25 30
 Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg
 35 40 45
 Gln Gly Gly Arg Thr Ser Ser Gln Arg Asp Pro Glu Pro Glu
 50 55 60
 Pro Glu Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn
 65 70 75 80
 Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr
 85 90 95
 Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp
 100 105 110
 Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys
 115 120 125

313

Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile
 130 135 140
 Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu
 145 150 155 160
 Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys
 165 170 175
 Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser
 180 185 190
 Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys
 195 200 205
 Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn Ser Tyr
 210 215 220
 Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro Ala Phe
 225 230 235 240
 Trp

<210> 843
 <211> 729
 <212> DNA
 <213> Homo sapiens

<400> 843
 atgcagcatc accaccatca ccacctcagg gttccggagc cgcggcccgg ggaggcgaaa 60
 gcggaggggg ccgcgcgcgc gaccccgctc aagccgctca cgtccttcct catccaggac 120
 atcctgcggg acggcgcgca gcggcaaggc ggccgcacga gcagccagag acagcgcgac 180
 ccggagccgg agccagagcc agagccagag ggaggacgca gccgcgccgg ggcgcagaac 240
 gaccagctga gcaccggggcc ccgcgcgcgc ccggatgagg ccgagacgct ggagagacc 300
 gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgcctt 360
 ccaaggcttc cccaaacccc taagcagccg cagaagcgct cccgagctgc cttctccac 420
 actcaggtga tcgagttgga gaggaagttc agccatcaga agtacctgtc ggcccctgaa 480
 cgggcccacc tggccaagaa cctcaagctc acggagaccc aagtgaagat atggttccag 540
 aacagacgct ataagactaa gcgaaagcag ctctcctcgg agctgggaga cttggagaag 600
 cactcctttt tgccggccct gaaagaggag gccttctccc gggcctccct ggtctccgtg 660
 tataacagct atccttacta ccatacctg cactgcgtgg gcagctggag cccagctttt 720
 tggtaatga 729

<210> 844
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 844
 ctactaagcg ctggagtgg ggatcag

27

<210> 845
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

314

<400> 845
catcgagaat tcactactct ctgactagat gtc

33

<210> 846
<211> 161
<212> PRT
<213> Homo sapiens

<400> 846
Met Gln His His His His His His Ala Gly Val Arg Asp Gln Gly Gln
1 5 10 15
Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly
20 25 30
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly
35 40 45
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys
50 55 60
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly
65 70 75 80
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val
85 90 95
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln
100 105 110
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro
115 120 125
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His
130 135 140
Gly Pro Pro Trp Leu Pro Asn Ala Leu Glu Arg Gly His Leu Val Arg
145 150 155 160
Glu

<210> 847
<211> 489
<212> DNA
<213> Homo sapiens

<400> 847
atgcagcatc accaccatca ccacgctgga gtgagggatc aggggcaggg cgcgagatgg 60
cctcacacag ggaagagagg gccctcctg cagggcctca cctgggccac aggaggacac 120
tgcttttctt ctgaggagtc aggagctgtg gatggtgctg gacagaagaa ggacagggcc 180
tggctcaggt gtccagaggc tgctgctggc ttccctttgg gatcagactg cagggaggga 240
gggcggcagg gttgtggggg gaggtagcat gaggatgacc tgggggtggc tccaggcctt 300
gccctgcct gggccctcac ccagcctccc tcacagtctc ctggccctca gtctctcccc 360
tccactccat cctccatctg gcctcagtgg gtcattctga tctactgaact gaccataccc 420
agccctgccc acggccctcc atggctcccc aatgccctgg agaggggaca tctagtcaga 480
gagtagtga 489

<210> 848
<211> 132
<212> PRT
<213> Homo sapiens

<400> 848
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe

315

1	5	10	15
Ala Ile Pro Ile Gly Gln Ala Met	Ala Ile Ala Gly Gln Ile Arg Ser		
	20	25	30
Gly Gly Gly Ser Pro Thr Val His	Ile Gly Pro Thr Ala Phe Leu Gly		
	35	40	45
Leu Gly Val Val Asp Asn Asn Gly	Asn Gly Ala Arg Val Gln Arg Val		
	50	55	60
Val Gly Ser Ala Pro Ala Ala Ser	Leu Gly Ile Ser Thr Gly Asp Val		
	65	70	75
Ile Thr Ala Val Asp Gly Ala Pro	Ile Asn Ser Ala Thr Ala Met Ala		
	85	90	95
Asp Ala Leu Asn Gly His His Pro	Gly Asp Val Ile Ser Val Asn Trp		
	100	105	110
Gln Thr Lys Ser Gly Gly Thr Arg	Thr Gly Asn Val Thr Leu Ala Glu		
	115	120	125
Gly Pro Pro Ala			
	130		

<210> 849

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 849

ggggaattca tcacctatgt gccgcctctg c

31

<210> 850

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 850

gggctcgagt cactcgccca cgaaatccgt gtaaaacagc

40

<210> 851

<211> 1203

<212> DNA

<213> Homo sapiens

<400> 851

atgcatcacc atcaccatca cacggccgog tccgataact tccagctgtc ccagggtggg 60
 cagggtattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
 accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180
 ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300
 gcgcttaacg ggcacatcc cggtagcgct atctcggtga cctggcaaac caagtcgggc 360
 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catcacctat 420
 gtgccgcctc tgctgctgga agtgggggta gaggagaagt tcatgaccat ggtgctgggc 480
 attggtccag tgctgggcct ggtctgtgtc ccgctcctag gctcagccag tgaccactgg 540
 cgtggacgct atggccgccc cgggcccttc atctgggcac tgtccttggg catcctgctg 600

316

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agcctctttc tcatcccaag ggccggctgg ctagcagggc tgctgtgccc ggatcccagg 660
cccctggagc tggcactgct catcctgggc gtggggctgc tggacttctg tggccagggtg 720
tgcttcactc cactggaggc cctgctctct gacctcttcc gggaccgcga cactgtcgc 780
caggcctact ctgtctatgc cttcatgac agtcttgggg gctgcctggg ctacctcctg 840
cctgccattg actgggacac cagtgcctg gcccctacc tgggcaccca ggaggagtgc 900
ctctttggcc tgctcaccct catcttcctc acctgcgtag cagccacact gctgggtggt 960
gaggaggcag cgctgggccc caccgagcca gcagaagggc tgtcggcccc ctccttgtcg 1020
ccccactgct gtccatgccg ggcccgttg gctttccgga acctgggcgc cctgcttccc 1080
cggctgcacc agctgtgctg cgcgatgcc cgcaccctgc gccggctctt cgtggctgag 1140
ctgtgcagct ggatggcact catgaccttc acgctgtttt acacggattt cgtgggcgag 1200
tga 1203

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<210> 852

<211> 400

<212> PRT

<213> Homo sapiens

<400> 852

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Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5              10              15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20              25              30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35              40              45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50              55              60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65              70              75              80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85              90              95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100             105             110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115             120             125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Ile Thr Tyr Val Pro Pro Leu
      130             135             140
Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr Met Val Leu Gly
      145             150             155             160
Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
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Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
      180             185             190
Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
      195             200             205
Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
      210             215             220
Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val
      225             230             235             240
Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro
      245             250             255
Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
      260             265             270
Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser
      275             280             285
Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu
      290             295             300
Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala
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317

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<210> 858

318

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27

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320

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321

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<400> 875

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<400> 876

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<210> 877

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<400> 877

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<210> 878

<211> 1195

<212> DNA

<213> Homo sapiens

<400> 878

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<212> PRT

<213> Homo sapiens

322

<400> 879

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Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35      40      45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50      55      60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65      70      75      80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85      90      95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100      105      110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115      120      125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130      135      140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145      150      155      160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165      170      175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180      185      190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195      200      205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210      215      220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
      225      230      235      240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
      245      250      255
Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
      260      265      270
Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
      275      280      285
Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
      290      295      300
Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
      305      310      315      320
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<211> 2172

<212> DNA

<213> Homo sapiens

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323

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<210> 881

<211> 2455

<212> DNA

<213> Homo sapiens

<400> 881

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<211> 2455

<212> DNA

<213> Homo sapiens

<400> 882

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325

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cttctcaaga gctaagaagg tttgctgagt attctggcat gatgtttggt gatcaaaca 2400
ctgctggcca aaaatgatga gtatttcccc ctcttgctga agatgtgctc catac 2455

```

<210> 883

<211> 62

<212> PRT

<213> Homo sapiens

<400> 883

```

Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
              5              10              15
His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
              20              25              30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
              35              40              45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
              50              55              60

```

<210> 884

<211> 135

<212> PRT

<213> Homo sapiens

<400> 884

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
              5              10              15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
              20              25              30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
              35              40              45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
              50              55              60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
              65              70              75              80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
              85              90              95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
              100              105              110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
              115              120              125
Leu Leu Asn Tyr Gln Val Ser
              130              135

```

<210> 885

<211> 77

<212> PRT

<213> Homo sapiens

<400> 885

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln

```

326

```

          5          10          15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
          20          25          30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
          35          40          45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
          50          55          60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
          65          70          75

```

<210> 886

<211> 60

<212> PRT

<213> Homo sapiens

<400> 886

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

<210> 887

<211> 76

<212> PRT

<213> Homo sapiens

<400> 887

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

<210> 888

<211> 76

<212> PRT

<213> Homo sapiens

<400> 888

```

Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
          5          10          15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
          20          25          30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
          35          40          45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
          50          55          60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
          65          70          75

```

327

<210> 889

<211> 80

<212> PRT

<213> Homo sapiens

<400> 889

```

Met Leu Leu His Ser Ser Leu Val Asn Arg Ala Arg Leu Cys Leu Lys
              5              10              15
Asn Lys Gln Ile Asn Lys Gln Thr Asn Lys Thr Glu Arg Phe Cys Cys
              20              25              30
Asn Val Gln Gly Ala Ile Cys Ser Phe Lys Lys Ile Ile Phe Gly Gln
              35              40              45
Ala Gln Trp Leu Thr Pro Val Ile Pro Ala Leu Trp Glu Ala Lys Val
              50              55              60
Gly Gly Ser Phe Glu Val Arg Ser Leu Arg Ser Ala Trp Pro Thr Trp
              65              70              75              80

```

<210> 890

<211> 72

<212> PRT

<213> Homo sapiens

<400> 890

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro His Asn Pro
              5              10              15
Ile Thr Ser His Gln Val Ser Ser Asp Thr Trp Asp Trp Val Gly Thr
              20              25              30
Gln Ser Gln Thr Val Ser Asp Ala Ala Gly Ala Gly Asp Thr Glu Thr
              35              40              45
Thr Gln Thr Trp Cys Leu Cys His Ser Ser Gly Leu Cys Leu Ser Pro
              50              55              60
Gly Pro Pro Ser Pro Ser Met Val
              65              70

```

<210> 891

<211> 77

<212> PRT

<213> Homo sapiens

<400> 891

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln
              5              10              15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
              20              25              30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
              35              40              45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
              50              55              60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
              65              70              75

```

<210> 892

<211> 60

<212> PRT

<213> Homo sapiens

<400> 892

328

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
 5 10 15
 Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
 20 25 30
 Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
 35 40 45
 Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
 50 55 60

<210> 893

<211> 76

<212> PRT

<213> Homo sapiens

<400> 893

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
 5 10 15
 Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
 20 25 30
 Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
 35 40 45
 Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
 50 55 60
 Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
 65 70 75

<210> 894

<211> 2479

<212> DNA

<213> Homo sapiens

<400> 894

gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac agcaagatgg 60
 ctttgaactc aggggtcacca ccagctattg gaccttacta tgaaaacccat ggataccaac 120
 cggaaaaccc ctatcccgcga cagcccactg tgggtcccccac tgtctacgag gtgcatccgg 180
 ctacgtacta cccgtccccc gtgccccagt acgccccgag ggtcctgacg caggcttcca 240
 acccgcgtcg ctgcacgcag cccaaatccc catccgggac agtgtgcacc tcaaagacta 300
 agaaagcact gtgcatcacc ttgaccctgg ggaccttcct cgtgggagct gcgctggccg 360
 ctggcctact ctggaagttc atgggcagca agtgcctcaa ctctgggata gagtgcgact 420
 cctcaggtac ctgcatcaac ccctctaact ggtgtgatgg cgtgtcacac tgccccggcg 480
 gggaggacga gaatcggtgt gttgcctctc acggaccaaa cttcatcctt cagatgtact 540
 catctcagag gaagtccctg caccctgtgt gccaaagacga ctggaacgag aactacgggc 600
 gggcggcctg cagggacatg ggctataaga ataattttta ctctagccaa ggaatagtgg 660
 atgacagcgg atccaccagc tttatgaaac tgaacacaag tgccggcaat gtcgatatct 720
 ataaaaaact gtaccacagt gatgcctgtt cttcaaaaagc agtgggtttct ttacgctggt 780
 tagcctgcgg ggtcaacttg aactcaagcc gccagagcag gatcgtgggc ggtgagagcg 840
 cgctcccggg ggccctggccc tggcaggtca gcctgcacgt ccagaacgtc cacgtgtgcg 900
 gaggtcccat catcaccccc gagtggatcg tgacagccgc ccactgcgtg gaaaaacctc 960
 ttaacaatcc atggcatttg acggcatttg cggggatttt gagacaatct ttcattgtct 1020
 atggagcccg ataccaagta caaaaagtga tttctcatcc aaattatgac tccaagacca 1080
 agaacaatga cattgcgctg atgaagctgc agaagcctct gactttcaac gacctagtga 1140
 aaccagtgtg tctgcccac ccaggcatga tgctgcagcc agaacagctc tgctggattt 1200
 ccgggtgggg ggccaccgag gagaaaggga agacctcaga agtgcgtgaac gctgccaagg 1260
 tgcttctcat tgagacacag agatgcaaca gcagatatgt ctatgacaac ctgatcacac 1320
 cagccatgat ctgtgccggc ttcttgccag ggaacgtcga ttcttgccag ggtgacagtg 1380
 gagggcctct ggtcacttcg aacaacaata tctggtggct gataggggat acaagctggg 1440
 gttctggtcg tgccaaagct tacagaccag gagtgtacgg gaatgtgatg gtattcacgg 1500
 actggattta tcgacaaatg aaggcaaacg gctaattccac atgggtcttcg tccttgacgt 1560

329

```

cgttttacaa gaaaacaatg gggctgggtt tgcttccccg tgcattgattt actcttagag 1620
atgattcaga ggtcacttca tttttattaa acagtgaact tgtctggctt tggcactctc 1680
tgccatactg tgcaggctgc agtggctccc ctgcccagcc tgctctccct aacccttgt 1740
ccgcaagggg tgatggccgg ctggttggtg gcactggcgg tcaattgtgg aaggaagagg 1800
gttggaggct gccccattg agatcttcct gctgagtcct ttccaggggc caattttgga 1860
tgagcatgga gctgtcactt ctcagctgct ggatgacttg agatgaaaaa ggagagacat 1920
ggaaagggag acagccaggt ggcacctgca ggggctgccc tctggggcca cttggtagt 1980
tccccagcct acttcacaag gggattttgc tgatgggttc ttagagcctt agcagccctg 2040
gatggtggcc agaaataaag ggaccagccc ttcatgggtg gtgacgtggg agtcacttgt 2100
aaggggaaca gaaacatttt tgttcttatg ggggtgagaat atagacagtg cccttgggtg 2160
gaggggaagca attgaaaagg aacttgccct gagcactcct ggtgcaggtc tccacctgca 2220
cattgggtgg ggtcctctgg agggagactc agccttcctc ctcactcctc ctgacctgca 2280
tcctagcacc ctggagagtg aatgcccctt ggtccctggc agggcgccaa gtttggcacc 2340
atgtcggcct cttcaggcct gatagtcatt ggaaattgag gtccatgggg gaaatcaagg 2400
atgctcagtt taaggtaacac tgtttccatg ttatgtttct acacattgat ggtggtgacc 2460
ctgagttcaa agccatctt                                     2479

```

<210> 895

<211> 492

<212> PRT

<213> Homo sapiens

<400> 895

```

Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
      5      10      15
Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100      105      110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115      120      125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130      135      140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145      150      155      160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165      170      175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180      185      190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195      200      205
Phe Met Lys Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys
      210      215      220
Leu Tyr His Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg
      225      230      235      240
Cys Leu Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
      245      250      255
Val Gly Gly Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser
      260      265      270
Leu His Val Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro

```


330

275	280	285
Glu Trp Ile Val Thr Ala Ala His Cys Val Glu Lys Pro Leu Asn Asn		
290	295	300
Pro Trp His Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met		
305	310	315
Phe Tyr Gly Ala Gly Tyr Gln Val Gln Lys Val Ile Ser His Pro Asn		
325	330	335
Tyr Asp Ser Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln		
340	345	350
Lys Pro Leu Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn		
355	360	365
Pro Gly Met Met Leu Gln Pro Glu Gln Leu Cys Trp Ile Ser Gly Trp		
370	375	380
Gly Ala Thr Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala		
385	390	395
Lys Val Leu Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr		
405	410	415
Asp Asn Leu Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly		
420	425	430
Asn Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser		
435	440	445
Asn Asn Asn Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly		
450	455	460
Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe		
465	470	475
Thr Asp Trp Ile Tyr Arg Gln Met Lys Ala Asn Gly		
485	490	

<210> 896

<211> 683

<212> DNA

<213> Homo sapiens

<400> 896

```

gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac agcaagatgg 60
ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat ggataccaac 120
cggaaaaccc ctatcccgcg cagcccactg tgggtccccc tgtctacgag gtgcatccgg 180
ctcagtacta cccgtccccc gtgccccagt acgccccgag ggtcctgacg caggcttcca 240
accccgtcgt ctgcacgcag cccaaatccc catccgggac agtgtgcacc tcaaagacta 300
agaaagcact gtgcatcacc ttgaccctgg ggaccttcct cgtgggagct gcgctggccg 360
ctggcctact ctggaagtgc atgggcagca agtgcctcaa ctctgggata gactgcgact 420
cctcaggtac ctgcatcaac cctctaaact ggtgtgatgg cgtgtcacac tgccccggcg 480
gggaggacga gaatcgggtg gttcgcctct acggacacaa cttcatcctt cagatgtact 540
catctcagag gaagtccctg caccctgtgt gccaaagacg ctggaacgag aactacgggc 600
gggcggcctg caggacatg ggctataaga ataattttta ctctagccaa ggaatagtgg 660
atgacagcgg atccaccagc ttt                                     683

```

<210> 897

<211> 209

<212> PRT

<213> Homo sapiens

<400> 897

```

Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
1           5           10           15

```

331

```

Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100      105      110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115      120      125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130      135      140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145      150      155      160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165      170      175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180      185      190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195      200      205
Phe

```

```

<210> 898
<211> 27
<212> PRT
<213> Homo sapiens

```

```

<400> 898
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
  1           5           10           15
Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg
      20      25

```

```

<210> 899
<211> 35
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> PCR primer

```

```

<400> 899
ggatccgccg ccaccatgtc actttctagc ctgct

```

35

```

<210> 900
<211> 27
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> PCR primer

```

```

<400> 900

```

332

gtcgactcag ctggaccaca gccgcag

27

<210> 901

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 901

ggatccgccg ccaccatggg ctgcaggctg ctct

34

<210> 902

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 902

gtcgactcag aaatcctttc tcttgac

27

<210> 903

<211> 936

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...()

<223> n = A,T,C or G

<400> 903

```

atgggctgca ggctgntctg ctgtgcggtt ctctgtctcc tgggagcggg ccccatggaa 60
acgggagtta cgcagacacc aagacacctg gtcattggaa tgacaaataa gaagtctttg 120
aaatgtgaac aacatctggg tcataacgct atgtattggg acaagcaaag tgctaagaag 180
ccactggagc tcatgtttgt ctacagtctt gaagaacggg ttgaaaacaa cagtgtgcca 240
agtcgcttct cacctgaatg ccccaacagc tctcaattat tccttcacct acacaccctg 300
cagccagaag actcggccct gtatctctgc gccagcagcc aagaccggac aagcagctcc 360
tacgagcagt acttcgggcc gggcaccagg ctacaggcca cagaggacct gaaaaacgtg 420
ttcccaccgg aggtcgctgt gtttgagcca tcagaagcag agatctccca caccctaaag 480
gccacactgg tgtgcctggc cacaggcttc taccctgacc acgtggagct gagctggtgg 540
gtgaatggga aggaggtgca cagtggggtc agcacagacc cgcagcccct caaggagcag 600
cccgccctca atgactccag atactgcctg agcagccgcc tgaggggtctc ggccaccttc 660
tggcagaacc cccgcaacca cttccgctgt caagtccagt tctacgggct ctcggagaat 720
gacgagtgga ccagggatag ggccaaacct gtcaccaga tcgtcagcgc cgaggcctgg 780
ggtagagcag actgtggctt cactccgag tcttaccagc aaggggtcct gtctgccacc 840
atcctctatg agatcttctg aggggaaggc acctgttatg ccgtgctggg cagtgccttc 900
gtgctgatgg ccatgggtcaa gagaaaggat ttctga 936

```

<210> 904

<211> 834

<212> DNA

<213> Homo sapiens

333

<220>

<221> misc_feature

<222> (1)...()

<223> n = A,T,C or G

<400> 904

```

atgtcacttt ctagcctgct naaggtgggc acagcttcac tgtggctagg acctggcatt 60
gccagaaga taactcaaac ccaaccagga atgttcgtgc aggaaaagga ggctgtgact 120
ctggactgca catatgacac cagtgatcaa agttatggtc tcttctggta caagcagccc 180
agcagtgagg aaatgatttt tcttatttat caggggtctt atgacgagca aaatgcaaca 240
gaaggtcgct actcattgaa tttccagaag gcaagaaaat ccgccaacct tgtcatctcc 300
gcttcacaac tgggggactc agcaatgtat ttctgtgcaa tgagagaggg cgcgggagga 360
ggaaacaaac tcacctttgg gacaggcact cagctaaaag tggaactcaa tatccagaac 420
cctgaccctg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgccta 480
ttcacccgatt ttgattctca aacaaatgtg tcacaaagta aggattctga tgtgtatatc 540
acagacaaaa ctgtgctaga catgaggtct atggacttca agagcaacag tgctgtggcc 600
tgagagcaaca aatctgactt tgcattgtga aacgccttca acaacagcat tattccagaa 660
gacaccttct tccccagccc agaaagtccc tgtgatgtca agctggtcga gaaaagcttt 720
gaaacagata cgaacctaaa ctttcaaaac ctgtcagtga ttgggttccg aatcctcctc 780
ctgaaagtgg ccgggtttaa tctgctcatg acgctgcggc tgtggtccag ctga 834

```

<210> 905

<211> 311

<212> PRT

<213> Homo sapiens

<220>

<221> variant

<222> (1)...(311)

<223> Xaa = Any amino acid

<400> 905

```

Met Gly Cys Arg Leu Xaa Cys Cys Ala Val Leu Cys Leu Leu Gly Ala
      5      10      15
Val Pro Met Glu Thr Gly Val Thr Gln Thr Pro Arg His Leu Val Met
      20      25      30
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Leu Gly His
      35      40      45
Asn Ala Met Tyr Trp Tyr Lys Gln Ser Ala Lys Lys Pro Leu Glu Leu
      50      55      60
Met Phe Val Tyr Ser Leu Glu Glu Arg Val Glu Asn Asn Ser Val Pro
      65      70      75      80
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser His Leu Phe Leu His
      85      90      95
Leu His Thr Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser
      100     105     110
Ser Gln Asp Arg Thr Ser Ser Ser Tyr Glu Gln Tyr Phe Gly Pro Gly
      115     120     125
Thr Arg Leu Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu
      130     135     140
Val Ala Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys
      145     150     155     160
Ala Thr Leu Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu
      165     170     175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr
      180     185     190
Asp Pro Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr
      195     200     205

```

334

Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro
 210 215 220
 Arg Asn His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn
 225 230 235 240
 Asp Glu Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser
 245 250 255
 Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr
 260 265 270
 Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly
 275 280 285
 Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala
 290 295 300
 Met Val Lys Arg Lys Asp Phe
 305 310

<210> 906

<211> 277

<212> PRT

<213> Homo sapiens

<400> 906

Met Ser Leu Ser Ser Leu Leu Lys Val Val Thr Ala Ser Leu Trp Leu
 5 10 15
 Gly Pro Gly Ile Ala Gln Lys Ile Thr Gln Thr Gln Pro Gly Met Phe
 20 25 30
 Val Gln Glu Lys Glu Ala Val Thr Leu Asp Cys Thr Tyr Asp Thr Ser
 35 40 45
 Asp Gln Ser Tyr Gly Leu Phe Trp Tyr Lys Gln Pro Ser Ser Gly Glu
 50 55 60
 Met Ile Phe Leu Ile Tyr Gln Gly Ser Tyr Asp Glu Gln Asn Ala Thr
 65 70 75 80
 Glu Gly Arg Tyr Ser Leu Asn Phe Gln Lys Ala Arg Lys Ser Ala Asn
 85 90 95
 Leu Val Ile Ser Ala Ser Gln Leu Gly Asp Ser Ala Met Tyr Phe Cys
 100 105 110
 Ala Met Arg Glu Gly Ala Gly Gly Gly Asn Lys Leu Thr Phe Gly Thr
 115 120 125
 Gly Thr Gln Leu Lys Val Glu Leu Asn Ile Gln Asn Pro Asp Pro Ala
 130 135 140
 Val Tyr Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu
 145 150 155 160
 Phe Thr Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser
 165 170 175
 Asp Val Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp
 180 185 190
 Phe Lys Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala
 195 200 205
 Cys Ala Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe
 210 215 220
 Pro Ser Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe
 225 230 235 240
 Glu Thr Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe
 245 250 255
 Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu
 260 265 270
 Arg Leu Trp Ser Ser
 275

<210> 907
 <211> 1536
 <212> DNA
 <213> Homo sapiens

<400> 907
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 atgtttcagc acctgatgca gaagcggaag cacaccaggt ggacgtatgg accactgacc 180
 tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300
 gagctggtga gcctcaagtg gaagcggtag ggcggccgt acttctgcat gctgggtgcc 360
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgccc cctcaagccc 420
 aggaccaata accgcacgag ccccggggac aacaccctct tacagcagaa gctacttcag 480
 gaagcctaca tgaccocctaa ggacgatata cggctggctg gggagctggt gactgtcatt 540
 ggggctatca tcatcctgct ggtagagggt ccagacatct tcagaatggg ggtcactcgc 600
 ttctttggac agaccatcct tgggggcccc ttccatgtcc tcatcatcac ctatgccttc 660
 atggtgctgg tgaccatggt gatgcggctc atcagtcca gcggggaggt ggtacccatg 720
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagg attccagatg 780
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900
 gaggaccccg aggagctagg ccacttctac gactaccca tggccctgtt cagcaccttc 960
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 gccagattg tggccaccac ggtgatgctg ggcggaagc tgctcgtctg cctgtggcct 1200
 cgctccggga tctgcggacg ggagtattgc ctgggagacc gctggttcct gcgggtggaa 1260
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 cccacactgt cccttcctat gccctcagtg tctcgaagta cctcccgag cagtccaat 1440
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 ctggaggacg gggagagctg ggaatatcag atctga 1536

<210> 908
 <211> 1533
 <212> DNA
 <213> Homo sapiens

<400> 908
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 atgtttcagc acctgatgca gaagcggaag cacaccaggt ggacgtatgg accactgacc 180
 tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300
 gagctggtga gcctcaagtg gaagcggtag ggcggccgt acttctgcat gctgggtgcc 360
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 aggaccaata accgcacgag ccccggggac aacaccctct tacagcagaa gctacttcag 480
 gaagcctaca tgaccocctaa ggacgatata cggctggctg gggagctggt gactgtcatt 540
 ggggctatca tcatcctgct ggtagagggt ccagacatct tcagaatggg ggtcactcgc 600
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 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagg attccagatg 780
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900
 gaggaccccg aggagctagg ccacttctac gactaccca tggccctgtt cagcaccttc 960
 gagctgttcc ttaccatcat cgatggcccc gccaaactaca acgtggacct gcccttcatt 1020
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080

336

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attgccatga tgggcgacac tcaactggcga gtggcccatg agcgggatga gctgtggagg 1140
gccagattg tggccaccac ggtgatgctg gagcgggaagc tgcctcgctg cctgtggcct 1200
cgctccggga tctgcggaag ggagtatggc ctgggagacc gctgggttcct gcgggtggaa 1260
gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacaccggg 1320
ggctctgagg atttgacaa agactcagtg gaaaaactag agctgggctg tcccttcagc 1380
ccccacctgt ccttcctat gccctcagtg tctogaagta cctccgcag cagtggcaat 1440
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ctggaggacg gggagagctg ggaatatcag atc 1533

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<210> 909

<211> 511

<212> PRT

<213> Homo sapiens

<400> 909

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Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
          20              25              30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
          35              40              45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
          50              55              60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
          65              70              75
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
          85              90              95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
          100             105             110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
          115             120             125
Phe Thr Met Cys Cys Ile Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn
          130             135             140
Arg Thr Ser Pro Arg Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln
          145             150             155
Glu Ala Tyr Met Thr Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu
          165             170             175
Val Thr Val Ile Gly Ala Ile Ile Ile Leu Leu Val Glu Val Pro Asp
          180             185             190
Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln Thr Ile Leu Gly
          195             200             205
Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe Met Val Leu Val
          210             215             220
Thr Met Val Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met
          225             230             235
Ser Phe Ala Leu Val Leu Gly Trp Cys Asn Val Met Tyr Phe Ala Arg
          245             250             255
Gly Phe Gln Met Leu Gly Pro Phe Thr Ile Met Ile Gln Lys Met Ile
          260             265             270
Phe Gly Asp Leu Met Arg Phe Cys Trp Leu Met Ala Val Val Ile Leu
          275             280             285
Gly Phe Ala Ser Ala Phe Tyr Ile Ile Phe Gln Thr Glu Asp Pro Glu
          290             295             300
Glu Leu Gly His Phe Tyr Asp Tyr Pro Met Ala Leu Phe Ser Thr Phe
          305             310             315
Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro Ala Asn Tyr Asn Val Asp
          325             330             335
Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala Ala Phe Ala Ile Ile Ala

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337

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          340          345          350
Thr Leu Leu Met Leu Asn Leu Leu Ile Ala Met Met Gly Asp Thr His
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Trp Arg Val Ala His Glu Arg Asp Glu Leu Trp Arg Ala Gln Ile Val
          370          375          380
Ala Thr Thr Val Met Leu Glu Arg Lys Leu Pro Arg Cys Leu Trp Pro
385          390          395          400
Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly Leu Gly Asp Arg Trp Phe
          405          410          415
Leu Arg Val Glu Asp Arg Gln Asp Leu Asn Arg Gln Arg Ile Gln Arg
          420          425          430
Tyr Ala Gln Ala Phe His Thr Arg Gly Ser Glu Asp Leu Asp Lys Asp
          435          440          445
Ser Val Glu Lys Leu Glu Leu Gly Cys Pro Phe Ser Pro His Leu Ser
          450          455          460
Leu Pro Met Pro Ser Val Ser Arg Ser Thr Ser Arg Ser Ser Ala Asn
465          470          475          480
Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg Arg Asp Leu Arg Gly Ile
          485          490          495
Ile Asn Arg Gly Leu Glu Asp Gly Glu Ser Trp Glu Tyr Gln Ile
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<210> 910

<211> 134

<212> PRT

<213> Homo sapiens

<400> 910

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Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
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Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
          20          25          30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
          35          40          45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
          50          55          60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
          65          70          75          80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
          85          90          95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
          100          105          110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
          115          120          125
Phe Thr Met Cys Cys Ile
          130

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<210> 911

<211> 55

<212> PRT

<213> Homo sapiens

<400> 911

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Ala Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn Arg Thr Ser Pro Arg
          5          10          15
Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln Glu Ala Tyr Met Thr
          20          25          30
Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu Val Thr Val Ile Gly

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338

35 40 45
 Ala Ile Ile Ile Leu Leu Val
 50 55

<210> 912
 <211> 39
 <212> PRT
 <213> Homo sapiens

<400> 912
 Glu Val Pro Asp Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln
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 Thr Ile Leu Gly Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe
 20 25 30
 Met Val Leu Val Thr Met Val
 35

<210> 913
 <211> 19
 <212> PRT
 <213> Homo sapiens

<400> 913
 Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met Ser Phe Ala
 5 10 15
 Leu Val Leu

<210> 914
 <211> 52
 <212> PRT
 <213> Homo sapiens

<400> 914
 Gly Trp Cys Asn Val Met Tyr Phe Ala Arg Gly Phe Gln Met Leu Gly
 5 10 15
 Pro Phe Thr Ile Met Ile Gln Lys Met Ile Phe Gly Asp Leu Met Arg
 20 25 30
 Phe Cys Trp Leu Met Ala Val Val Ile Leu Gly Phe Ala Ser Ala Phe
 35 40 45
 Tyr Ile Ile Phe
 50

<210> 915
 <211> 213
 <212> PRT
 <213> Homo sapiens

<400> 915
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 5 10 15
 Ala Leu Phe Ser Thr Phe Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro
 20 25 30
 Ala Asn Tyr Asn Val Asp Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala
 35 40 45
 Ala Phe Ala Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Leu Ile Ala
 50 55 60
 Met Met Gly Asp Thr His Trp Arg Val Ala His Glu Arg Asp Glu Leu

339

65					70					75				80
Trp	Arg	Ala	Gln	Ile	Val	Ala	Thr	Thr	Val	Met	Leu	Glu	Arg	Lys
				85					90					95
Pro	Arg	Cys	Leu	Trp	Pro	Arg	Ser	Gly	Ile	Cys	Gly	Arg	Glu	Tyr
			100					105					110	
Leu	Gly	Asp	Arg	Trp	Phe	Leu	Arg	Val	Glu	Asp	Arg	Gln	Asp	Leu
		115					120					125		Asn
Arg	Gln	Arg	Ile	Gln	Arg	Tyr	Ala	Gln	Ala	Phe	His	Thr	Arg	Gly
		130					135					140		Ser
Glu	Asp	Leu	Asp	Lys	Asp	Ser	Val	Glu	Lys	Leu	Glu	Leu	Gly	Cys
		145				150				155				Pro
Phe	Ser	Pro	His	Leu	Ser	Leu	Pro	Met	Pro	Ser	Val	Ser	Arg	Ser
				165					170					Thr
Ser	Arg	Ser	Ser	Ala	Asn	Trp	Glu	Arg	Leu	Arg	Gln	Gly	Thr	Leu
				180					185				190	Arg
Arg	Asp	Leu	Arg	Gly	Ile	Ile	Asn	Arg	Gly	Leu	Glu	Asp	Gly	Glu
		195					200					205		Ser
Trp	Glu	Tyr	Gln	Ile										
				210										

<210> 916

<211> 1302

<212> DNA

<213> Homo sapiens

<400> 916

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ttcatcctaa taggcctccc tggtttagaa gaggctcagt tctggttggc cttcccattg 180
tgctccctct accttattgc tgtgctaggt aacttgacaa tcatctacat tgtgcggact 240
gagcacagcc tgcattgagcc catgtatata tttctttgca tgctttcagg cattgacatc 300
ctcatctcca cctcatccat gcccaaaatg ctggccatct tctggttcaa ttccactacc 360
atccagtttg atgcttgtct gctacagatg tttgccatcc actccttacc tggcatggaa 420
tccacagtgc tgctggccat ggcttttgac cgctatgtgg ccatctgtca cccactgcgc 480
catgccacag tacttacgtt gcctcgtgtc accaaaattg gtgtggctgc tgtggtgcgg 540
ggggctgcac tgatggcacc ccttctgtc ttcatcaagc agctgccctt ctgccgctcc 600
aatatccttt ccattccta ctgcctacac caagatgtca tgaagctggc ctgtgatgat 660
atccgggtca atgtcgtcta tggccttacc gtcacatct cgcctattgg cctggactca 720
cttctcatct ccttctcata tctgcttatt cttaagactg tgttgggctt gacacgtgaa 780
gccaggcca aggcatttg cacttgctc tctcatgtgt gtgctgtgtt catattctat 840
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cccgatctct tggccaatat ctatctgctg gttcctcctg tgcacacccc aattgtctat 960
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gcttcagagc cctaggtgtc agtgatcaaa cttcttttcc attcagagtc ctctgattca 1080
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acaactcaga tccttcaaat atgaaactgg ttggggaatc tccatttttt caatattatt 1200
ttcttcttgg ttttcttgct acatataatt attaatatccc tgactagggt gtggttttag 1260
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<210> 917

<211> 2061

<212> DNA

<213> Homo sapiens

<400> 917

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gtgtcagtga tcaaacttct tttccattca gagtctcttg attcagattt taatgttaac 120

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at t t t t g g a a g   a c a g t a t t c a   g a a a a a a a t   t t c c t t a a t a   a a a a t a c a a c   t c a g a t c c t t   180
c a a a t a t g a a   a c t g g t t g g g   g a a t c t c c a t   t t t t t c a a t a   t t a t t t t c t t   c t t t g t t t t c   240
t t g c t a c a t a   t a a t t a t t a a   t a c c c t g a c t   a g g t t g t g g t   t g g a g g g t t a   t t a c t t t t c a   300
t t t t a c c a t g   c a g t c c a a a t   c t a a a c t g c t   t c t a c t g a t g   g t t t a c a g c a   t t c t g a g a t a   360
a g a a t g g t a c   a t c t a g a g a a   c a t t t g c c a a   a g g c c t a a g c   a c g g c a a a g g   a a a a t a a a c a   420
c a g a a t a t a a   t a a a a t g a g a   t a a t c t a g c t   t a a a a c t a t a   a c t t c c t c t t   c a g a a c t c c c   480
a a c c a c a t t g   g a t c t c a g a a   a a a t g c t g t c   t t c a a a a t g a   c t t c t a c a g a   g a a g a a a t a a   540
t t t t t c t c t c t   g g a c a c t a g c   a c t t a a g g g g   a a g a t t g g a a   g t a a a g c c t t   g a a a a g a g t a   600
c a t t t a c c t a   c g t t a a t g a a   a g t t g a c a c a   c t g t t c t g a g   a g t t t t c a c a   g c a t a t g g a c   660
c c t g t t t t t c   c t a t t t a a t t   t t c t t a t c a a   c c c t t t a a t t   a g g c a a a g a t   a t t a t t a g t a   720
c c c t c a t t g t   a g c c a t g g g a   a a a t t g a t g t   t c a g t g g g g a   t c a g t g a a t t   a a a t g g g g t c   780
a t a c a a g t a t   a a a a a t t a a a   a a a a a a g g a c   t t c a t g c c c a   a t c t c a t a t g   a t g t g g a a g a   840
a c t g t t a g a g   a g a c c a a c a g   g g t a g t g g g t   t a g a g a t t t c   c a g a g t c t t a   c a t t t t c t a g   900
a g g a g g t a t t   t a a t t t c t t c   t c a c t c a t c c   a g t g t t g t a t   t t a g g a a t t t   c c t g g c a a c a   960
g a a c t c a t g g   c t t t a a t c c c   a c t a g c t a t t   g c t t a t t g t c   c t g g t c c a a t   t g c c a a t t a c   1020
c t g t g t c t t g   g a a g a a g t g a   t t t c t a g g t t   c a c c a t t a t g   g a a g a t t c t t   a t t c a g a a a g   1080
t c t g c a t a g g   g c t t a t a g c a   a g t t a t t t a t   t t t t a a a a g t   t c c a t a g g t g   a t t c t g a t a g   1140
g c a g t g a g g t   t a g g g a g c c a   c c a g t t a t g a   t g g g a a g t a t   g g a a t g g c a g   g t c t t g a a g a   1200
t a a c a t t g g c   c t t t t g a g t g   t g a c t c g t a g   c t g g a a a g t g   a g g g a a t c t t   c a g g a c c a t g   1260
c t t t a t t t g g   g g c t t t g t g c   a g t a t g g a a c   a g g g a c t t t g   a g a c c a g g a a   a g c a a t c t g a   1320
c t t a g g c a t g   g g a a t c a g g c   a t t t t t g c t t   c t g a g g g g c t   a t t a c c a a g g   g t t a a t a g g t   1380
t t c a t c t t c a   a c a g g a t a t g   a c a a c a g t g t   t a a c c a a g a a   a c t c a a a t t a   c a a a t a c t a a   1440
a a c a t g t g a t   c a t a t a t g t g   g t a a g t t t c a   t t t t c t t t t t   c a a t c c t c a g   g t t c c c t g a t   1500
a t g g a t t c c t   a t a a c a t g c t   t t c a t c c c c t   t t t g t a a t g g   a t a t c a t a t t   t g g a a t g c c   1560
t a t t t a a t a c   t t g t a t t t g c   t g c t g g a c t g   t a a g c c c a t g   a g g g c a c t g t   t t a t t a t t g a   1620
a t g t c a t c t c   t g t t c a t c a t   t g a c t g c t c t   t t g c t c a t c a   t t g a a t c c c c   c a g c a a a g t g   1680
c c t a g a a c a t   a a t a g t g c t t   a t g c t t g a c a   c c g g t t a t t t   t t c a t c a a a c   c t g a t t c c t t   1740
c t g t c c t g a a   c a c a t a g c c a   g g c a a t t t t c   c a g c c t t c t t   t g a g t t g g g t   a t t a t t a a a t   1800
t c t g g c c a t t   a c t t c c a a t g   t g a g t g g a a g   t g a c a t g t g c   a a t t t c t a t a   c c t g g c t c a t   1860
a a a a c c c t c c   c a t g t g c a g c   c t t t c a t g t t   g a c a t t a a a t   g t g a c t t g g g   a a g c t a t g t g   1920
t t a c a c a g a g   t a a a t c a c c a   g a a g c c t g g a   t t t c t g a a a a   a a c t g t g c a g   a g c c a a a c c t   1980
c t g t c a t t t g   c a a c t c c c a c   t t g t a t t t g t   a c g a g g c a g t   t g g a t a a g t g   a a a a t a a a g   2040
t a c t a t t g t g   t c a a g t c t c t   g                                     2061

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<210> 918

<211> 957

<212> DNA

<213> Homo sapiens

<400> 918

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a t g a t g g t g g   a t c c c a a t g g   c a a t g a a t c c   a g t g c t a c a t   a c t t c a t c c t   a a t a g g c c t c   60
c c t g g t t t a g   a a g a g g c t c a   g t t c t g g t t g   g c c t t c c c a t   t g t g c t c c c t   c t a c c t t a t t   120
g c t g t g c t a g   g t a a c t t g a c   a a t c a t c t a c   a t t g t g c g g a   c t g a g c a c a g   c c t g c a t g a g   180
c c c a t g t a t a   t a t t t c t t t g   c a t g c t t t c a   g g c a t t g a c a   t c c t c a t c t c   c a c c t c a t c c   240
a t g c c c a a a a   t g c t g g c c a t   c t t c t g g t t c   a a t t c c a c t a   c c a t c c a g t t   t g a t g c t t g t   300
c t g c t a c a g a   t g t t t g c c a t   c c a c t c c t t a   t c t g g c a t g g   a a t c c a c a g t   g c t g c t g g c c   360
a t g g c t t t t g   a c c g c t a t g t   g g c c a t c t g t   c a c c c a c t g c   g c c a t g c c a c   a g t a c t t a c g   420
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c c c c t t c c t g   t c t t c a t c a a   g c a g c t g c c c   t t c t g c c g c t   c c a a t a t c c t   t t c c c a t t c c   540
t a c t c c c t a c   a c c a a g a t g t   c a t g a a g c t g   g c c t g t g a t g   a t a t c c g g g t   c a a t g t c g t c   600
t a t g g c c t t a   t c g t c a t c a t   c t c o g c c a t t   g g c c t g g a c t   c a c t t t c t c a t   c t c c t t c t c a   660
t a t c t g c t t a   t t o t t a a g a c   t g t g t t g g g c   t t g a c a c g t g   a a g c c c a g g c   c a a g g c a t t t   720
g g c a c t t g c g   t c t c t c a t g t   g t g t g c t g t g   t t c a t a t t c t   a t g t a c c t t t   c a t t g g a t t g   780
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a t t c g a c a g c   g c a t c c t t c g   a c t t t t c c a t   g t g g c c a c a c   a c g c t t c a g a   g c c c t a g   957

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341

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 <213> Homo sapiens

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 Phe Leu Cys Met Leu Ser Gly Ile Asp Ile Leu Ile Ser Thr Ser Ser
 65 70 75 80
 Met Pro Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln
 85 90 95
 Phe Asp Ala Cys Leu Leu Gln Met Phe Ala Ile His Ser Leu Ser Gly
 100 105 110
 Met Glu Ser Thr Val Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala
 115 120 125
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 130 135 140
 Thr Lys Ile Gly Val Ala Ala Val Val Arg Gly Ala Ala Leu Met Ala
 145 150 155 160
 Pro Leu Pro Val Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile
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 195 200 205
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342

Gly Thr Cys Val Ser His Val Cys Ala Val Phe Ile Phe Tyr Val Pro
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<211> 28

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<400> 921

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<213> Homo sapiens

343

<400> 925

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<211> 22

<212> PRT

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<212> DNA

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344

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3245

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<211> 1479

<212> DNA

<213> Homo sapiens

<400> 930

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345

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<210> 931

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<212> DNA

<213> Homo sapiens

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<211> 492

<212> PRT

<213> Homo sapiens

<400> 932

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Val	Pro	Thr	Val	Tyr	Glu	Val	His	Pro	Ala	Gln	Tyr	Tyr	Pro	Ser	Pro
Val	Pro	Gln	Tyr	Ala	Pro	Arg	Val	Leu	Thr	Gln	Ala	Ser	Asn	Pro	Val
Val	Cys	Thr	Gln	Pro	Lys	Ser	Pro	Ser	Gly	Thr	Val	Cys	Thr	Ser	Lys
Thr	Lys	Lys	Ala	Leu	Cys	Ile	Thr	Leu	Thr	Leu	Gly	Thr	Phe	Leu	Val
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Cys	Ser	Asn	Ser	Gly	Ile	Glu	Cys	Asp	Ser	Ser	Gly	Thr	Cys	Ile	Asn
Pro	Ser	Asn	Trp	Cys	Asp	Gly	Val	Ser	His	Cys	Pro	Gly	Gly	Glu	Asp
Glu	Asn	Arg	Cys	Val	Arg	Leu	Tyr	Gly	Ser	Asn	Phe	Ile	Leu	Gln	Val
Tyr	Ser	Ser	Gln	Arg	Lys	Ser	Trp	His	Pro	Val	Cys	Gln	Asp	Asp	Trp
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347

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 <212> PRT
 <213> Homo sapiens

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 Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
 50 55 60
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 <211> 393
 <212> PRT
 <213> Homo sapiens

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 Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp Asn Glu Asn
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 Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn Asn Phe Tyr
 85 90 95
 Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser Phe Met Lys
 100 105 110
 Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys Leu Tyr His
 115 120 125
 Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg Cys Ile Ala
 130 135 140
 Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile Val Gly Gly
 145 150 155 160
 Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser Leu His Val
 165 170 175
 Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro Glu Trp Ile
 180 185 190

348

Val Thr Ala Ala His Cys Val Glu Lys, Pro Leu Asn Asn Pro Trp His
 195 200 205
 Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met Phe Tyr Gly
 210 215 220
 Ala Gly Tyr Gln Val Glu Lys Val Ile Ser His Pro Asn Tyr Asp Ser
 225 230 235 240
 Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln Lys Pro Leu
 245 250 255
 Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn Pro Gly Met
 260 265 270
 Met Leu Gln Pro Glu Gln Leu Cys Trp Ile Ser Gly Trp Gly Ala Thr
 275 280 285
 Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala Lys Val Leu
 290 295 300
 Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr Asp Asn Leu
 305 310 315 320
 Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly Asn Val Asp
 325 330 335
 Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser Lys Asn Asn
 340 345 350
 Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly Cys Ala Lys
 355 360 365
 Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe Thr Asp Trp
 370 375 380
 Ile Tyr Arg Gln Met Arg Ala Asp Gly
 385 390

<210> 935
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR Primer

<400> 935
 gtgctgtggg agtccccgcg gc 22

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 <212> DNA
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<220>
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<400> 936
 cgtgaactcg agtcattaga ttaacctcgt ggacgc 36

<210> 937
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR Primer

349

<400> 937
gtgctgtggg agtccccgcg gc

22

<210> 938
<211> 1158
<212> DNA
<213> Homo sapiens

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tggacacttt gcgagggtt ttgctggctg ctgctgctgc ccgtcatgct actcatcgta 120
gcccccccg tgaagctcgc tgctttccct acctccttaa gtgactgcca aacgcccacc 180
ggctggaatt gctctgggta tgatgacaga gaaaatgatc tcttcctctg tgacaccaac 240
acctgtaaat ttgatgggga atgtttaaga attggagaca ctgtgacttg cgtctgtcag 300
ttcaagtgca acaatgacta tgtgcctgtg tgtgggtcca atggggagag ctaccagaat 360
gagtgttacc tgcgacaggc tgcattgcaa cagcagagtg agatacttgt ggtgtcagaa 420
ggatcatgtg ccacagatgc aggatcagga tctggagatg gattccatga aggtctctga 480
gaaactagtc aaaaggagac atccaactgt gatatttgcc agtttggtgc agaattgtac 540
gaagatgccg aggatgtctg gtgtgtgtgt aatattgact gttctcaaac caacttcaat 600
ccccctctgc cttctgatgg gaaatcttat gataatgcat gccaaatcaa agaagcatcg 660
tgtcagaaac aggagaaaat tgaagtcatt tctttgggtc gatgtcaaga taacacaact 720
acaactacta agtctgaaga tgggcattat gcaagaacag attatgcaga gaattgtaac 780
aaattagaag aaagtgccag agaaccaccac ataccttgtc cggaacatta caatggcttc 840
tgcattgcag ggaagtgtga gcattctatc aatatgcagg agccatcttg cagggtgtgat 900
gctgggtata ctggacaaca ctgtgaaaaa aaggactaca gtgttctata cgttggtccc 960
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gtcatctgtg ttggtggctc ctgcatcaca aggaaatgcc ccagaagcaa cagaattcac 1080
agacagaagc aaaatacagg gcactacagt tcagacaata caacaagagc gtccacgagg 1140
ttaatctaag gactcgag 1158

<210> 939
<211> 1020
<212> DNA
<213> Homo sapiens

<400> 939
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gaatgtttta gaattggaga cactgtgact tgcgtctgtc agttcaagtg caacaatgac 180
tatgtgcctg tgtgtggctc caatggggag agctaccaga atgagtgtta cctgcgacag 240
gctgcatgca aacagcagag tgagatactt gtggtgtcag aaggatcatg tgccacagat 300
gcaggatcag gatctggaga tggagtccat gaaggctctg gagaaactag tcaaaaggag 360
acatccacct gtgatatttg ccagtttggt gcagaatgtg acgaagatgc cgaggatgtc 420
tgggtgtgtg gtaatatattg ctgttctcaa accaacttca atccccctct cgcttctgat 480
gggaaatctt atgataatgc atgccaatc aaagaagcat cgtgtcagaa acaggagaaa 540
attgaagtca tgtctttggg tcgatgtcaa gataacacaa ctacaactac taagtctgaa 600
gatgggcatt atgcaagaac agattatgca agaatgtcta acaaataga agaaagtgc 660
agagaacacc acataccttg tccggaacat tacaatggct tctgcatgca tgggaagtgt 720
gagcattcta tcaatatgca ggagccatct tgcaggtgtg atgctgggta tactggacaa 780
cactgtgaaa aaaaggacta cagtgttcta tacgttgttc ccggtcctgt acgatttcag 840
tatgtcttaa tcgcagctgt gattggaaca attcagattg ctgtcatctg tgtgggtggc 900
ctctgcatca caaggaaatg cccagaagc aacagaattc acagacagaa gcaaaatata 960
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<210> 940
<211> 336

350

<212> PRT

<213> Homo sapiens

<400> 940

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Met Gln His His His His His His Asp Cys Gln Thr Pro Thr Gly Trp
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Asn Cys Ser Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp
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Thr Asn Thr Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr
                35              40              45
Val Thr Cys Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val
                50              55              60
Cys Gly Ser Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln
                65              70              75              80
Ala Ala Cys Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser
                85              90              95
Cys Ala Thr Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly
                100             105             110
Ser Gly Glu Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln
                115             120             125
Phe Gly Ala Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys
                130             135             140
Asn Ile Asp Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp
                145             150             155             160
Gly Lys Ser Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln
                165             170             175
Lys Gln Glu Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn
                180             185             190
Thr Thr Thr Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp
                195             200             205
Tyr Ala Glu Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His
                210             215             220
Ile Pro Cys Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys
                225             230             235             240
Glu His Ser Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly
                245             250             255
Tyr Thr Gly Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val
                260             265             270
Val Pro Gly Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile
                275             280             285
Gly Thr Ile Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr
                290             295             300
Arg Lys Cys Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr
                305             310             315             320
Gly His Tyr Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
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<210> 941

<211> 381

<212> PRT

<213> Homo sapiens

<400> 941

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Met Gln His His His His His His Val Leu Trp Glu Ser Pro Arg Gln
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Cys Ser Ser Trp Thr Leu Cys Glu Gly Phe Cys Trp Leu Leu Leu Leu
                20              25              30

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351

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Pro Val Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe
      35      40      45
Pro Thr Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser
      50      55      60
Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr
      65      70      75      80
Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys
      85      90      95
Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser
      100      105      110
Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys
      115      120      125
Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr
      130      135      140
Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu
      145      150      155      160
Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala
      165      170      175
Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp
      180      185      190
Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser
      195      200      205
Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu
      210      215      220
Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr
      225      230      235      240
Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu
      245      250      255
Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys
      260      265      270
Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser
      275      280      285
Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly
      290      295      300
Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly
      305      310      315      320
Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile
      325      330      335
Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys
      340      345      350
Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr
      355      360      365
Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      370      375      380

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<210> 942

<211> 45

<212> DNA

<213> Homo sapiens

<400> 942

ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaac

45

<210> 943

<211> 15

<212> PRT

<213> Homo sapiens

<400> 943

Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys Val Asn
5 10 15

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